SIGNAL GENETICS, INC.
Form 424B3
January 09, 2017
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Filed Pursuant to Rule 424(b)(3)
Registration No. 333-214893

PROPOSED MERGER

YOUR VOTE IS VERY IMPORTANT

To the Stockholders of Signal Genetics, Inc. and Miragen Therapeutics, Inc.:

Signal Genetics, Inc., or Signal, and Miragen Therapeutics, Inc., or Miragen, entered into an Agreement and Plan of Merger and Reorganization on October 31, 2016, or the Merger Agreement, pursuant to which a wholly-owned subsidiary of Signal will merge with and into Miragen, with Miragen surviving as a wholly-owned subsidiary of Signal, which is referred to as the Merger. Miragen and Signal believe that the Merger will result in a clinical-stage biopharmaceutical company that discovers and develops proprietary RNA-targeted therapeutics with a specific focus on microRNAs and their role in diseases where there is a high unmet medical need.

Immediately prior to the effective time of the Merger, each share of Miragen preferred stock will be converted into one share of Miragen s common stock, or Miragen common stock, as determined in accordance with the Miragen certificate of incorporation then in effect. At the effective time of the Merger, each share of Miragen common stock will be converted into the right to receive a fraction of a share of Signal common stock, or the Exchange Ratio. It is currently anticipated that, at the closing of the Merger, the Exchange Ratio would be approximately 0.6995 pre-split shares of Signal s common stock, or Signal common stock, and would be within a range of approximately 0.6995 to 0.0466 post-split shares of Signal common stock. Signal will assume (i) each outstanding warrant to purchase Miragen capital stock, which will be converted into warrants to purchase Signal common stock and (ii) each outstanding and unexercised option to purchase Miragen common stock, which will be converted into options to purchase Signal common stock. Signal stockholders will continue to own and hold their existing shares of Signal common stock. The Exchange Ratio is determined pursuant to a formula in the Merger Agreement and described in the attached proxy statement/prospectus/information statement, and these estimates are subject to adjustment.

Immediately after the Merger, Miragen securityholders will own approximately 96% of the fully-diluted common stock of the combined company, with Signal securityholders, whose shares of Signal common stock will remain outstanding after the Merger, owning approximately 4% of the fully-diluted common stock of the combined company, each assuming that Miragen closes its concurrent financing immediately prior to the effective time of the Merger. If the concurrent financing does not close, then Miragen securityholders would own approximately 94% of the fully-diluted common stock of the combined company and Signal securityholders would own approximately 6% of the fully-diluted common stock of the combined company. These estimates are based on the anticipated pre-split Exchange Ratio and post-split Exchange Ratios and are subject to adjustment.

Shares of Signal common stock are currently listed on The NASDAQ Capital Market under the symbol SGNL. Signal has filed an initial listing application for the combined company with The NASDAQ Capital Market. After completion of the Merger, Signal will be renamed Miragen Therapeutics, Inc. and expects to trade on The NASDAQ Capital

Market under the symbol MGEN. On January 5, 2017, the last trading day before the date of this proxy statement/prospectus/information statement, the closing sale price of Signal common stock was $5.33 per share.

Signal is holding a special meeting of stockholders, or the Signal special meeting, in order to obtain the stockholder approvals necessary to complete the Merger and related matters. At the Signal special meeting, which will be held at 12255 El Camino Real, Suite 300, San Diego, California 92130, at 9:00 a.m., local time, on February 10, 2017, unless postponed or adjourned to a later date, Signal will ask its stockholders to, among other things:

- approve the issuance of shares of Signal common stock to Miragen stockholders pursuant to the terms of the Merger Agreement;

- approve the change in control of Signal resulting from the Merger;

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approve the conversion of the Unsecured Demand Promissory Note, dated March 6, 2015, issued by Signal to Bennett LeBow in the original principal amount of $1,105,009, as amended on October 31, 2016, into shares of Signal common stock;

approve the Signal 2016 Equity Incentive Plan;

approve the Signal 2016 Employee Stock Purchase Plan;

approve an amendment to the certificate of incorporation of Signal changing the Signal corporate name to Miragen Therapeutics, Inc. ;

approve an amendment to the certificate of incorporation of Signal effecting a reverse stock split of Signal s issued and outstanding common stock within a range of every one to 15 shares (or any number in between) of outstanding Signal common stock being combined and reclassified into one share of Signal common stock;

approve an amendment to the certificate of incorporation of Signal increasing the authorized common stock from 50,000,000 to 100,000,000 shares;

approve the sale of all of Signal s intellectual property assets related to its MyPRS test to Quest Diagnostics Investments LLC pursuant to an intellectual property purchase agreement;

approve an amendment to the certificate of incorporation of Signal to eliminate the ability of Signal stockholders to act by written consent;

consider and vote upon an adjournment of the Signal special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of the proposals set forth above; and

transact such other business as may properly come before the stockholders at the Signal special meeting or any adjournment or postponement thereof.

As described in the accompanying proxy statement/prospectus/information statement, certain Miragen stockholders who in the aggregate own approximately 78% of the outstanding shares of Miragen common stock on an as-converted to common stock basis, and certain Signal stockholders who in the aggregate own 26% of the outstanding shares of Signal common stock, are parties to support agreements with Signal and Miragen, respectively, whereby such stockholders agreed to vote in favor of certain proposals described in this proxy statement/prospectus/information statement, subject to the terms of the support agreements.

In addition, following the registration statement on Form S-4, of which this proxy statement/prospectus/information statement is a part, being declared effective by the Securities and Exchange Commission, or the SEC, and pursuant to

the conditions of the Merger Agreement, the Miragen stockholders who are party to the support agreements will each execute an action by written consent of the Miragen stockholders, referred to herein as the written consent, adopting the Merger Agreement, thereby approving the Merger and related transactions. These stockholders hold a sufficient number of shares of Miragen capital stock to adopt the Merger Agreement, and no meeting of Miragen stockholders to adopt the Merger Agreement and approve the Merger and related transactions will be held. Nevertheless, all Miragen stockholders will have the opportunity to elect to adopt the Merger Agreement, thereby approving the Merger and related transactions, by signing and returning to Miragen a written consent.

After careful consideration, the Signal and Miragen boards of directors have approved the Merger Agreement and the respective proposals described in this proxy statement/prospectus/information statement, and each of the Signal and Miragen boards of directors has determined that it is advisable to consummate the Merger. Signal s board of directors recommends that its stockholders vote FOR the proposals described in the accompanying proxy statement/prospectus/information statement, and Miragen s board of directors recommends that its stockholders sign and return the written consent to Miragen indicating their approval of the Merger and adoption of the Merger Agreement and related transactions.

More information about Signal, Miragen and the Merger is contained in this proxy statement/prospectus/information statement. Signal and Miragen urge you to read the accompanying proxy statement/

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prospectus/information statement carefully and in its entirety. IN PARTICULAR, YOU SHOULD CAREFULLY CONSIDER THE MATTERS DISCUSSED UNDER RISK FACTORS BEGINNING ON PAGE 19.

Signal and Miragen are excited about the opportunities the Merger brings to both Signal s and Miragen s stockholders, and thank you for your consideration and continued support.

Samuel D. Riccitelli
President and Chief Executive Officer
Signal Genetics, Inc.

William S. Marshall, Ph.D.
President and Chief Executive Officer
Miragen Therapeutics, Inc.

Neither the SEC nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this proxy statement/prospectus/information statement. Any representation to the contrary is a criminal offense.

The accompanying proxy statement/prospectus/information statement is dated January 9, 2017, and is first being mailed to Signal and Miragen stockholders on or about January 17, 2017.

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SIGNAL GENETICS, INC.

5740 FLEET STREET

CARLSBAD, CALIFORNIA 92008

(760) 537-4100

NOTICE OF SPECIAL MEETING OF STOCKHOLDERS

To Be Held On February 10, 2017

Time: 9:00 a.m., local time
Date: Friday, February 10, 2017
Place: 12255 El Camino Real, Suite 300, San Diego, California 92130
Purposes:

1. To approve the issuance of shares of common stock of Signal Genetics, Inc. (Signal) to stockholders of Miragen Therapeutics, Inc. (Miragen) pursuant to the terms of the Agreement and Plan of Merger and Reorganization between Signal, Miragen and Signal Merger Sub, Inc., dated October 31, 2016, a copy of which is attached as *Annex A*, which is referred to as the Merger Agreement;

2. To approve the change in control of Signal resulting from the merger contemplated by the Merger Agreement;

3. To approve the conversion of the Unsecured Demand Promissory Note, dated March 6, 2015, issued by Signal to Bennett LeBow in the original principal amount of $1,105,009, as amended on October 31, 2016 into shares of Signal common stock;

4. To approve the Signal 2016 Equity Incentive Plan, a copy of which is attached as *Annex B*;

5. To approve the Signal 2016 Employee Stock Purchase Plan, a copy of which is attached as *Annex C*;

6. To approve an amendment to the certificate of incorporation of Signal changing the Signal corporate name to Miragen Therapeutics, Inc. in the form attached as *Annex D*;

7. To approve an amendment to the certificate of incorporation of Signal effecting a reverse stock split of Signal s issued and outstanding common stock within a range of every one to 15 shares (or any number in

between) of outstanding Signal common stock being combined and reclassified into one share of Signal common stock in the form attached as *Annex E*;

8. To approve an amendment to the certificate of incorporation of Signal increasing the number of authorized shares of Signal common stock from 50,000,000 shares to 100,000,000 shares in the form attached as *Annex F*;

9. To approve the sale of all of Signal s intellectual property assets related to its MyPRS test to Quest Diagnostics Investments LLC pursuant to an intellectual property purchase agreement, a copy of which is attached as *Annex G*;

10. To approve an amendment to the certificate of incorporation of Signal to eliminate the ability of Signal stockholders to act by written consent in the form attached as *Annex H*;

11. To consider and vote upon an adjournment of the Signal special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of the proposals set forth above; and

12. To transact such other business as may properly come before the stockholders at the Signal special meeting or any adjournment or postponement thereof.

Record Date: Signal s board of directors has fixed January 9, 2017 as the record date for the determination of stockholders entitled to notice of, and to vote at, the Signal special meeting and any adjournment or postponement thereof. Only holders of record of shares of Signal common stock at the close of business on the record date are entitled to notice of, and to vote at, the Signal special meeting. At the close of business on the record date, Signal had 742,293 shares of common stock outstanding and entitled to vote.

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Your vote is important. The affirmative vote of the holders of a majority of the shares of Signal common stock having voting power present in person or represented by proxy at the Signal special meeting, assuming a quorum is present, is required for approval of Signal Proposal Nos. 1, 2, 3, 4, 5 and 11. The affirmative vote of the holders of a majority of outstanding shares of Signal common stock entitled to vote on the record date for the Signal special meeting is required for approval of Signal Proposal Nos. 6, 7, 8, 9 and 10. Each of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9 are conditioned upon each other and the approval of each such proposal is a condition to the completion of the Merger. Therefore, the Merger cannot be consummated without the approval of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9.

Even if you plan to attend the Signal special meeting in person, Signal requests that you sign and return the enclosed proxy to ensure that your shares will be represented at the Signal special meeting if you are unable to attend. You may change or revoke your proxy at any time before it is voted at the Signal special meeting.

SIGNAL S BOARD OF DIRECTORS HAS DETERMINED AND BELIEVES THAT EACH OF THE PROPOSALS OUTLINED ABOVE IS FAIR TO, IN THE BEST INTERESTS OF, AND ADVISABLE TO SIGNAL AND ITS STOCKHOLDERS AND HAS APPROVED EACH SUCH PROPOSAL. SIGNAL S BOARD OF DIRECTORS RECOMMENDS THAT SIGNAL STOCKHOLDERS VOTE FOR EACH SUCH PROPOSAL.

By Order of Signal s Board of Directors,

Samuel D. Riccitelli

President and Chief Executive Officer

Carlsbad, California

January 9, 2017

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REFERENCES TO ADDITIONAL INFORMATION

This proxy statement/prospectus/information statement incorporates important business and financial information about Signal that is not included in or delivered with this document. You may obtain this information without charge through the SEC website (*www.sec.gov*) or upon your written or oral request by contacting the chief financial officer of Signal Genetics, Inc., 5740 Fleet Street, Carlsbad, California 92008 or by calling (760) 537-4100.

To ensure timely delivery of these documents, any request should be made no later than February 1, 2017 to receive them before the special meeting.

For additional details about where you can find information about Signal, please see the section titled *Where You Can Find More Information* in this proxy statement/prospectus/information statement.

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QUESTIONS AND ANSWERS ABOUT THE MERGER

Except where specifically noted, the following information and all other information contained in this proxy statement/prospectus/information statement gives effect to Signal s one-for-15 reverse stock split of its common stock, which was effective at 5:01 p.m. Eastern Time on November 4, 2016, but does not give effect to the proposed reverse stock split described in Signal Proposal No. 7, beginning on page 167 in this proxy statement/prospectus/information statement.

The following section provides answers to frequently asked questions about the Merger. This section, however, provides only summary information. For a more complete response to these questions and for additional information, please refer to the cross-referenced sections.

Q: What is the Merger?

A: Signal Genetics, Inc., or Signal, and Miragen Therapeutics, Inc., or Miragen, have entered into an Agreement and Plan of Merger and Reorganization, dated October 31, 2016, or the Merger Agreement. The Merger Agreement contains the terms and conditions of the proposed business combination of Signal and Miragen. Under the Merger Agreement, Signal Merger Sub, Inc., a wholly-owned subsidiary of Signal, or Merger Sub, will merge with and into Miragen, with Miragen surviving as a wholly-owned subsidiary of Signal. After the completion of the Merger, Signal will change its corporate name to Miragen Therapeutics, Inc. as required by the Merger Agreement. This transaction is referred to as the Merger.

Immediately prior to the effective time of the Merger, each share of Miragen preferred stock will be converted into one share of Miragen s common stock, or Miragen common stock, as determined in accordance with the Miragen certificate of incorporation then in effect. At the effective time of the Merger, each share of Miragen common stock will be converted into the right to receive a fraction of a share of Signal common stock, or the Exchange Ratio. It is currently anticipated that, at the closing of the Merger, the Exchange Ratio would be approximately 0.6995 pre-split shares of Signal s common stock, or Signal common stock, and would be within a range of approximately 0.6995 to 0.0466 post-split shares of Signal common stock. Signal will assume (i) each outstanding warrant to purchase Miragen capital stock, which will be converted into warrants to purchase Signal common stock and (ii) each outstanding and unexercised option to purchase Miragen common stock, which will be converted into options to purchase Signal common stock. Signal stockholders will continue to own and hold their existing shares of Signal common stock. The Exchange Ratio is determined pursuant to a formula in the Merger Agreement and described in this proxy statement/prospectus/information statement, and these estimates are subject to adjustment.

Immediately after the Merger, Miragen securityholders will own approximately 96% of the fully-diluted common stock of the combined company, with Signal securityholders, whose shares of Signal common stock will remain outstanding after the Merger, owning approximately 4% of the fully-diluted common stock of the combined company, each assuming that Miragen closes its concurrent financing immediately prior to the effective time of the Merger. If the concurrent financing does not close, then Miragen securityholders would own approximately 94% of the fully-diluted common stock of the combined company and Signal securityholders would own approximately 6% of the fully-diluted common stock of the combined company. These estimates are based on the anticipated pre-split Exchange Ratio and post-split Exchange Ratios and are subject to adjustment.

The rules applicable to the calculation of the Exchange Ratio, which are described in the sections titled *The Merger Merger Consideration and Exchange Ratio* beginning on page 113 and *The Merger Agreement Merger Consideration and Exchange Ratio* beginning on page 123, are complex and circumstances as of the effective time of the Merger may result in an Exchange Ratio that differs from estimates in this proxy

statement/prospectus/information statement.

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Q: What will happen to Signal if, for any reason, the Merger does not close?

A: If, for any reason, the Merger does not close, Signal s board of directors may elect to, among other things, dissolve or liquidate its assets, attempt to complete another strategic transaction like the Merger, attempt to sell or otherwise dispose of the various assets of Signal or continue to operate the business of Signal. If Signal decides to dissolve and liquidate its assets, Signal would be required to pay all of its debts and contractual obligations, and to set aside certain reserves for potential future claims, and there can be no assurances as to the amount or timing of available cash left, if any, to distribute to stockholders after paying the debts and other obligations of Signal and setting aside funds for reserves.

Q: Why are the two companies proposing to merge?

A: Following the Merger, Signal and Miragen believe that the Merger will result in a clinical-stage biopharmaceutical company that discovers and develops proprietary RNA-targeted therapeutics with a specific focus on microRNAs and their role in diseases where there is a high unmet medical need. Signal and Miragen believe that the combined company will have the following potential advantages: (i) a diversified, clinical stage product development pipeline; (ii) appropriate resources; (iii) an experienced management team; and (iv) the potential to access additional sources of capital.

Q: Why am I receiving this proxy statement/prospectus/information statement?

A: You are receiving this proxy statement/prospectus/information statement because you have been identified as a stockholder of Signal or Miragen as of the applicable record date, and you are entitled, as applicable, to vote at Signal s special meeting of stockholders to approve the matters set forth above, or to sign and return the Miragen written consent to adopt and approve the matters set forth in the written consent. This document serves as:

a proxy statement of Signal used to solicit proxies for its special meeting of stockholders to vote on the matters set forth above;

a prospectus of Signal used to offer shares of Signal common stock in exchange for shares of Miragen common stock in the Merger and issuable upon exercise of Miragen options and Miragen warrants; and

an information statement of Miragen used to solicit the written consent of its stockholders for approval of matters relating to the Merger.

Q: What is required to consummate the Merger?

A: To consummate the Merger, Signal stockholders must approve the proposal numbers 1 through 9. Pursuant to the terms of the Merger Agreement, Signal is also requesting that Signal stockholders approve proposal numbers 10 and 11 below, which are, collectively with proposal numbers 1 through 9, referred to as the Signal Proposals. The Signal Proposals include the following matters:

1.

the issuance of shares of Signal common stock to Miragen stockholders pursuant to the terms of the Agreement and Plan of Merger and Reorganization between Signal, Miragen and Signal Merger Sub, Inc., dated October 31, 2016, a copy of which is attached as *Annex A*, which is referred to as the Merger Agreement;

2. the change in control of Signal resulting from the Merger contemplated by the Merger Agreement;

3. the conversion of the Unsecured Demand Promissory Note, dated March 6, 2015, issued by Signal to Bennett LeBow in the original principal amount of $1,105,009, as amended on October 31, 2016, which is referred to as the Note, into shares of Signal common stock;

4. the Signal 2016 Equity Incentive Plan, a copy of which is attached as *Annex B*;

5. the Signal 2016 Employee Stock Purchase Plan, a copy of which is attached as *Annex C*;

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6. an amendment to the certificate of incorporation of Signal changing the Signal corporate name to Miragen Therapeutics, Inc. in the form attached as *Annex D*;

7. an amendment to the certificate of incorporation of Signal effecting a reverse stock split of Signal s issued and outstanding common stock within a range of every one to 15 shares (or any number in between) of outstanding Signal common stock being combined and reclassified into one share of Signal common stock in the form attached as *Annex E*, which is referred to as the reverse stock split;

8. an amendment to the certificate of incorporation of Signal increasing the number of authorized shares of Signal common stock from 50,000,000 shares to 100,000,000 shares in the form attached as *Annex F*;

9. the sale of all of Signal s intellectual property assets related to its MyPRS test to Quest Diagnostics Investments LLC pursuant to an intellectual property purchase agreement, a copy of which is attached as *Annex G*;

10. an amendment to the certificate of incorporation of Signal to eliminate the ability of Signal stockholders to act by written consent in the form attached as *Annex H*; and

11. to consider and vote on an adjournment of the Signal special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of the proposals set forth above.

The presence, in person or represented by proxy, at the Signal special meeting of the holders of a majority of the shares of Signal common stock outstanding and entitled to vote at the Signal special meeting is necessary to constitute a quorum at the meeting. Abstentions and broker non-votes will be counted towards a quorum. The affirmative vote of the holders of a majority of the shares of Signal common stock having voting power present in person or represented by proxy at the Signal special meeting, assuming a quorum is present, is required for approval of Signal Proposal Nos. 1, 2, 3, 4, 5 and 11. The affirmative vote of the holders of a majority of shares of Signal common stock entitled to vote on the record date for the Signal special meeting is required for approval of Signal Proposal Nos. 6, 7, 8, 9 and 10. Each of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9 are conditioned upon each other and the approval of each such proposal is a condition to the completion of the Merger. Therefore, the Merger cannot be consummated without the approval of Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9.

Votes will be counted by the inspector of election appointed for the meeting, who will separately count FOR and AGAINST votes, abstentions and broker non-votes. Abstentions will be counted towards the vote total for each proposal and will have the same effect as AGAINST votes for Signal Proposal Nos. 6, 7, 8, 9 and 10, but will have no effect on Signal Proposal Nos. 1, 2, 3, 4, 5 and 11. Similarly, broker non-votes will have the same effect as AGAINST votes for Signal Proposal Nos. 6, 7, 8, 9 and 10, but will have no effect on Signal Proposal Nos. 1, 2, 3, 4, 5 and 11.

As of December 31, 2016, the directors and executive officers of Signal owned or controlled 26% of the outstanding shares of Signal common stock entitled to vote at the Signal special meeting. The directors and executive officers of Signal owning these shares are subject to support agreements. Each Signal stockholder that entered into a support agreement has agreed to vote all shares of Signal common stock owned by him as of the record date in favor of the Signal Proposals and against any acquisition proposal, as defined in the Merger Agreement.

The adoption of the Merger Agreement and the approval of the Merger and related transactions by the stockholders of Miragen require the affirmative votes of the holders of (i) a majority of the outstanding Miragen common stock and preferred stock, voting together as one class on an as-converted to common stock basis and (ii) 70% of the shares of Miragen preferred stock, voting together as one class on an as-converted to common stock basis. In addition to the requirement of obtaining such stockholder approvals, each of the other closing conditions set forth in the Merger Agreement must be satisfied or waived.

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In addition, following the registration statement on Form S-4, of which this proxy statement/prospectus/information statement is a part, being declared effective by the SEC and pursuant to the conditions of the Merger Agreement, Miragen stockholders who are party to the support agreements will each execute written consents approving the Merger and related transactions. These stockholders hold a sufficient number of shares of Miragen capital stock to adopt the Merger Agreement, and no meeting of Miragen stockholders to adopt the Merger Agreement and approve the Merger and related transactions will be held. Stockholders of Miragen, including those who are parties to support agreements, are being requested to execute written consents providing such approvals.

For a more complete description of the closing conditions under the Merger Agreement, you are urged to read the section titled *The Merger Agreement Conditions to the Completion of the Merger* in this proxy statement/prospectus/information statement.

Q: What will Miragen stockholders, warrantholders and optionholders receive in the Merger?

A: As a result of the Merger, Miragen securityholders will become entitled to receive shares of Signal common stock equal to approximately 96% of the outstanding common stock of the combined company, assuming that Miragen closes its concurrent financing immediately prior to the effective time of the Merger. If the concurrent financing does not close, then Miragen securityholders will become entitled to receive shares of Signal common stock equal to approximately 94% of the fully-diluted common stock of the combined company. Each of Miragen s outstanding warrants to purchase shares of Miragen capital stock not terminated or exercised at or prior to the effective time of the Merger will be converted into a warrant to purchase Signal common stock, with the number of shares and exercise price being appropriately adjusted to reflect the Exchange Ratio between Signal common stock and Miragen common stock determined in accordance with the Merger Agreement. Following the closing of the Merger, Miragen s optionholders will have each Miragen option converted into an option to purchase Signal common stock, with the number of shares and exercise price being appropriately adjusted to reflect the Exchange Ratio between Signal common stock and Miragen common stock determined in accordance with the Merger Agreement.

For a more complete description of what Miragen stockholders, warrantholders and optionholders will receive in the Merger, please see the sections titled *Market Price and Dividend Information* and *The Merger Agreement Merger Consideration and Exchange Ratio* in this proxy statement/prospectus/information statement.

Q: Who will be the directors of Signal following the Merger?

A: Immediately following the Merger, Signal s board of directors is expected to be composed of seven directors to be designated solely by Miragen, including the following: William S. Marshall, Ph.D., Bruce L. Booth, Ph.D., John W. Creecy, Thomas E. Hughes, Ph.D., Kevin Koch, Ph.D., Kyle A. Lefkoff and Joseph L. Turner.

Q: Who will be the executive officers of Signal immediately following the Merger?

A: Immediately following the Merger, the executive management team of Signal is expected to be composed solely of the members of the Miragen executive management team prior to the Merger, as set forth below:

Name	**Title**
William S. Marshall, Ph.D.	President and Chief Executive Officer
Jason A. Leverone	Chief Financial Officer, Secretary and Treasurer
Adam S. Levy	Chief Business Officer

Paul D. Rubin, M.D. Executive Vice President, Research and Development

Q: As a Signal stockholder, how does Signal s board of directors recommend that I vote?

A: After careful consideration, Signal s board of directors recommends that Signal stockholders vote FOR all of the Signal Proposals.

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Q: As a Miragen stockholder, how does Miragen s board of directors recommend that I vote?

A: After careful consideration, Miragen s board of directors recommends that Miragen stockholders execute the written consent indicating their vote in favor of the adoption of the Merger Agreement and the approval of the Merger and the transactions contemplated thereby.

Q: What risks should I consider in deciding whether to vote in favor of the Merger or to execute and return the written consent, as applicable?

A: You should carefully review the section of this proxy statement/prospectus/information statement titled *Risk Factors* beginning on page 19, which sets forth certain risks and uncertainties related to the Merger, risks and uncertainties to which the combined company s business will be subject, and risks and uncertainties to which each of Signal and Miragen, as an independent company, is subject.

Q: When do you expect the Merger to be consummated?

A: The Merger is anticipated to occur as early as the first quarter of 2017 after the Signal special meeting to be held on February 10, 2017, but the exact timing cannot be predicted. For more information, please see the section titled *The Merger Agreement Conditions to the Completion of the Merger* in this proxy statement/prospectus/information statement.

Q: What do I need to do now?

A: Signal and Miragen urge you to read this proxy statement/prospectus/information statement carefully, including its annexes, and to consider how the Merger affects you.

If you are a Signal stockholder of record, you may provide your proxy instructions in one of four different ways. First, you can attend the Signal special meeting in person and Signal will provide you with a ballot when you arrive at the meeting. Second, you can mail your signed proxy card in the enclosed return envelope. Third, you can provide your proxy instructions via telephone by following the instructions on your proxy card. Fourth, you can provide your proxy instructions via the Internet by following the instructions on your proxy card. If you hold your shares in street name (as described below), you may provide your proxy instructions via telephone or the internet by following the instructions on your vote instruction form. Please provide your proxy instructions only once, unless you are revoking a previously delivered proxy instruction, and as soon as possible so that your shares can be voted at the special meeting of Signal stockholders.

If you are a stockholder of Miragen, you may execute and return your written consent to Miragen in accordance with the instructions provided.

Q: What happens if I do not return a proxy card or otherwise provide proxy instructions, as applicable?

A: If you are a Signal stockholder, the failure to return your proxy card or otherwise provide proxy instructions will reduce the aggregate number of votes required to approve Signal Proposals Nos. 1, 2, 3, 4, 5 and 11 and will have the same effect as voting against 6, 7, 8, 9 and 10. Also, your shares will not be counted for purposes of determining whether a quorum is present at the Signal special meeting.

Q: May I vote in person at the special meeting of stockholders of Signal?

A: If your shares of Signal common stock are registered directly in your name with Signal s transfer agent, you are considered to be the stockholder of record with respect to those shares, and the proxy materials and proxy card are being sent directly to you by Signal. If you are a Signal stockholder of record, you may attend the special meeting of Signal stockholders and vote your shares in person. Even if you plan to attend the Signal special meeting in person, Signal requests that you sign and return the enclosed proxy to ensure that your shares will be represented at the Signal special meeting if you are unable to attend.

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If your shares of Signal common stock are held in a brokerage account or by another nominee, you are considered the beneficial owner of shares held in street name, and the proxy materials are being forwarded to you by your broker or other nominee together with a voting instruction card. As the beneficial owner, you are also invited to attend the special meeting of Signal stockholders. Because a beneficial owner is not the stockholder of record, you may not vote these shares in person at the Signal special meeting unless you obtain a legal proxy from the broker, trustee or nominee that holds your shares, giving you the right to vote the shares at the meeting.

Q: When and where is the special meeting of Signal stockholders being held?

A: The special meeting of Signal stockholders will be held at 12255 El Camino Real, Suite 300, San Diego, California 92130, at 9:00 a.m., local time, on February 10, 2017. Subject to space availability, all Signal stockholders as of the record date, or their duly appointed proxies, may attend the meeting. Since seating is limited, admission to the meeting will be on a first-come, first-served basis.

Q: If my Signal shares are held in street name by my broker, will my broker vote my shares for me?

A: Unless your broker has discretionary authority to vote on certain matters, your broker will not be able to vote your shares of Signal common stock on matters requiring discretionary authority without instructions from you. If you do not give instructions to your broker, your broker can vote your Signal shares with respect to discretionary items but not with respect to non-discretionary items. Discretionary items are proposals considered routine under the rules of The NASDAQ Capital Market on which your broker may vote shares held in street name in the absence of your voting instructions. On non-discretionary items for which you do not give your broker instructions, the Signal shares will be treated as broker non-votes. It is anticipated that Signal Proposal Nos. 1, 2, 3, 6, 7, 8, 9 and 10 will be non-discretionary items. To make sure that your vote is counted, you should instruct your broker to vote your shares, following the procedures provided by your broker.

Q: May I change my vote after I have submitted a proxy or provided proxy instructions?

A: Signal stockholders of record, other than those Signal stockholders who are parties to support agreements, may change their vote at any time before their proxy is voted at the Signal special meeting in one of three ways. First, a stockholder of record of Signal can send a written notice to the Secretary of Signal stating that it would like to revoke its proxy. Second, a stockholder of record of Signal can submit new proxy instructions either on a new proxy card or via the Internet. Third, a stockholder of record of Signal can attend the Signal special meeting and vote in person. Attendance alone will not revoke a proxy. If a Signal stockholder who owns Signal shares in street name has instructed a broker to vote its shares of Signal common stock, the stockholder must follow directions received from its broker to change those instructions.

Q: Who is paying for this proxy solicitation?

A: Signal and Miragen will share equally the cost of printing and filing of this proxy statement/prospectus/information statement and the proxy card. Arrangements will also be made with brokerage firms and other custodians, nominees and fiduciaries who are record holders of Signal common stock for the forwarding of solicitation materials to the beneficial owners of Signal common stock. Signal will reimburse these brokers, custodians, nominees and fiduciaries for the reasonable out-of-pocket expenses they incur in connection with the forwarding of solicitation materials. Signal has retained Advantage Proxy to assist it in soliciting proxies using the means referred to above. Signal will pay the fees of Advantage Proxy, which Signal expects to be approximately $7,500, plus reimbursement of out-of-pocket expenses.

Q: What are the material U.S. federal income tax consequences of the reverse stock split to Signal stockholders?

A: The reverse stock split described in Signal Proposal No. 7 should constitute a recapitalization for U.S. federal income tax purposes. As a result, a U.S. Holder (as described in more detail in the section titled *Matters*

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Being Submitted to a Vote of Signal Stockholders Signal Proposal No. 7: Approval of the Amendment of the Certificate of Incorporation of Signal Effecting the Reverse Stock Split Material U.S. Federal Income Tax Consequences of the Reverse Stock Split) of Signal common stock generally should not recognize gain or loss upon such reverse stock split, except with respect to cash received in lieu of a fractional share of Signal common stock, as discussed below in the section titled *Matters Being Submitted to a Vote of Signal Stockholders Signal Proposal No. 7: Approval of the Amendment of the Certificate of Incorporation of Signal Effecting the Reverse Stock Split Material U.S. Federal Income Tax Consequences of the Reverse Stock Split Cash in Lieu of Fractional Shares* . A U.S. Holder s aggregate tax basis in the shares of Signal common stock received pursuant to such reverse stock split should equal the aggregate tax basis of the shares of the Signal common stock surrendered (excluding any portion of such basis that is allocated to any fractional share of Signal common stock), and such U.S. Holder s holding period in the shares of Signal common stock received should include the holding period in the shares of Signal common stock surrendered. Treasury Regulations provide detailed rules for allocating the tax basis and holding period of the shares of Signal common stock surrendered to the shares of Signal common stock received in a recapitalization pursuant to such reverse stock split. U.S. Holders of shares of Signal common stock acquired on different dates and at different prices should consult their tax advisors regarding the allocation of the tax basis and holding period of such shares. For more information, please see the section titled *Matters Being Submitted to a Vote of Signal Stockholders Signal Proposal No. 7: Approval of the Amendment of the Certificate of Incorporation of Signal Effecting the Reverse Stock Split Material U.S. Federal Income Tax Consequences of the Reverse Stock Split* on page 167.

Q: What are the material U.S. federal income tax consequences of the Merger to Miragen stockholders?

A: Each of Signal and Miragen intends the Merger to qualify as a reorganization within the meaning of Section 368(a) of the Internal Revenue Code of 1986, as amended, or the Code. In general, and subject to the qualifications and limitations set forth in the section titled *The Merger Material U.S. Federal Income Tax Consequences of the Merger*, if the Merger qualifies as a reorganization within the meaning of Section 368(a) of the Code, the material tax consequences to U.S. Holders of Miragen common stock will be as follows:

- a Miragen stockholder will not recognize gain or loss upon the exchange of Miragen common stock for Signal common stock pursuant to the Merger, except to the extent of cash received in lieu of a fractional share of Miragen common stock as described below;
- a Miragen stockholder who receives cash in lieu of a fractional share of Signal common stock in the Merger will recognize capital gain or loss in an amount equal to the difference between the amount of cash received in lieu of a fractional share and the stockholder s tax basis allocable to such fractional share;
- a Miragen stockholder s aggregate tax basis for the shares of Signal common stock received in the Merger (including any fractional share interest for which cash is received) will equal the stockholder s aggregate tax basis in the shares of Miragen common stock surrendered in the Merger; and
- the holding period of the shares of Signal common stock received by a Miragen stockholder in the Merger will include the holding period of the shares of Miragen common stock surrendered in exchange therefor.

Tax matters are very complicated, and the tax consequences of the Merger to a particular Miragen stockholder will depend on such stockholder s circumstances. Accordingly, you are strongly urged to consult your tax advisor for a full

understanding of the tax consequences of the Merger to you, including the applicability and effect of federal, state, local and non-U.S. income and other tax laws. For more information, please see the section titled *The Merger Material U.S. Federal Income Tax Consequences of the Merger* beginning on page 115.

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Q: Who can help answer my questions?

A: If you are a Signal stockholder and would like additional copies of this proxy statement/prospectus/information statement without charge or if you have questions about the Merger, including the procedures for voting your shares, you should contact:

ADVANTAGE PROXY

Telephone: (877) 870-8565 (toll free); (206) 870-8565 (collect)

Email: ksmith@advantageproxy.com

If you are a Miragen stockholder and would like additional copies of this proxy statement/prospectus/information statement without charge or if you have questions about the Merger, including the procedures for voting your shares, you should contact:

Miragen Therapeutics, Inc.

6200 Lookout Road

Boulder, CO 80301

Telephone: (720) 407-4595

Attn: Investor Relations

Email: investorrelations@miragenrx.com

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PROSPECTUS SUMMARY

This summary highlights selected information from this proxy statement/prospectus/information statement and may not contain all of the information that is important to you. To better understand the Merger, the proposals being considered at the Signal special meeting and the Miragen stockholder actions that are the subject of the written consent, you should read this entire proxy statement/prospectus/information statement carefully, including the Merger Agreement and the other annexes to which you are referred herein. For more information, please see the section titled Where You Can Find More Information in this proxy statement/prospectus/information statement. Except where specifically noted, the following information and all other information contained in this proxy statement/prospectus/information statement gives effect to Signal s one-for-15 reverse stock split of its common stock, which was effective at 5:01 p.m. Eastern Time on November 4, 2016, but does not give effect to the proposed reverse stock split described in Signal Proposal No. 7, beginning on page 167 in this proxy statement/prospectus/information statement.

The Companies

Signal Genetics, Inc.

5740 Fleet Street

Carlsbad, CA 92008

(760)-537-4100

Signal is a commercial stage, molecular genetic diagnostic company focused on providing innovative diagnostic services that help physicians in the care of their patients suffering from multiple myeloma. Its MyPRS test, a microarray-based gene expression profile assay, is performed in Signal s laboratory located in Little Rock, Arkansas, which is certified under the Clinical Laboratory Improvement Amendments of 1988 and accredited by the College of American Pathologists. Signal is licensed to sell MyPRS in all 50 states. Since its inception, Signal has operated at a loss as it built the infrastructure to support the growing customer base for MyPRS. Due to current market conditions, Signal s current liquidity position and its depressed stock price, it has (i) entered into the Merger Agreement and (ii) entered into an intellectual property purchase agreement to sell all of Signal s intellectual property assets related to its MyPRS assay to Quest Diagnostics Investments LLC.

Miragen Therapeutics, Inc.

6200 Lookout Road

Boulder, CO 80301

(303) 531-5952

Miragen is 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. Miragen believes its 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. Miragen uses its expertise in systems biology and oligonucleotide chemistry to discover and develop a pipeline of product candidates. Miragen s two lead product candidates, MRG-106 and MRG-201, are currently in Phase 1 clinical trials. Miragen s 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. Miragen s 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 Miragen s clinical programs, it is developing a pipeline of pre-clinical product

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candidates. The goal of Miragen s 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) and safety of the product candidate in pre-clinical studies.

Signal Merger Sub, Inc.

5740 Fleet Street

Carlsbad, CA 92008

(760)-537-4100

Merger Sub is a wholly-owned subsidiary of Signal and was formed solely for the purpose of carrying out the Merger.

The Merger (see page 88)

If the Merger is completed, Merger Sub will merge with and into Miragen, with Miragen surviving as a wholly-owned subsidiary of Signal.

Immediately prior to the effective time of the Merger, each share of Miragen preferred stock will be converted into one share of Miragen s common stock, or Miragen common stock, as determined in accordance with the Miragen certificate of incorporation then in effect. At the effective time of the Merger, each share of Miragen common stock will be converted into the right to receive a fraction of a share of Signal common stock, or the Exchange Ratio. It is currently anticipated that, at the closing of the Merger, the Exchange Ratio would be approximately 0.6995 pre-split shares of Signal common stock and would be within a range of approximately 0.6995 and 0.0466 post-split shares of Signal common stock. The Exchange Ratio is determined pursuant to a formula in the Merger Agreement and described in this proxy statement/prospectus/information statement and these estimates are subject to adjustment. At the effective time of the Merger, each outstanding option and warrant, whether or not vested, to purchase shares of Miragen capital stock unexercised immediately prior to the effective time of the Merger will be converted into an option or warrant to purchase shares of Signal common stock. All rights with respect to each Miragen option or warrant will be assumed by Signal in accordance with its terms. Accordingly, from and after the effective time of the Merger, each option or warrant assumed by Signal may be exercised solely for shares of Signal common stock.

Each share of Signal common stock issued and outstanding at the time of the Merger will remain issued and outstanding and those shares will be unaffected by the Merger. Signal warrants that are unexercised immediately prior to the effective time of the Merger will remain outstanding. Signal stock options and restricted stock units that are not exercised or settled, as applicable, prior to the effective time of the Merger will be cancelled and terminated upon the effectiveness of the Merger. Please see *The Merger Stock Options and Warrants* beginning on page 114.

For a more complete description of the Exchange Ratio, please see the section titled *The Merger Agreement Merger Consideration and Exchange Ratio* beginning on page 123.

The Merger will be completed as promptly as practicable after all of the conditions to completion of the Merger are satisfied or waived, including the approval of the stockholders of Signal and Miragen. Signal and Miragen are working to complete the Merger as quickly as practicable. However, Signal and Miragen cannot predict the exact timing of the completion of the Merger because it is subject to various conditions. After completion of the Merger, assuming that Signal receives the required stockholder approval of Signal Proposal No. 6, Signal will be renamed Miragen Therapeutics, Inc.

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Reasons for the Merger (see pages 95 and 98)

Following the Merger, the combined company will be a clinical-stage biopharmaceutical company that discovers and develops proprietary RNA-targeted therapeutics with a specific focus on microRNAs and their role in diseases where there is a high unmet medical need. Signal and Miragen believe that the combined company will have the following potential advantages:

- the combined company will be a publicly traded, clinical-stage company with a diversified development portfolio of two well-characterized compounds addressing novel targets for several distinct diseases, as well as a pipeline of RNA targeted therapeutic candidates;

- the combined company will be led by an experienced senior management team from Miragen and a board of directors of seven members designated by Miragen; and

- Miragen has commitments for $40.7 million to fund Miragen s development pipeline from an investor syndicate that includes some of Miragen s existing stockholders and new investors. Although not a condition to the completion of the Merger, if closed the investment, in addition to Miragen s $16.1 million sale of its Series C convertible preferred stock in September 2016, is expected to provide sufficient funding to advance Miragen s clinical development programs. Each of Miragen s clinical programs has the potential, if successful, to create value for the stockholders of the combined company and present the combined company with additional fund raising opportunities in the future.

Each of the board of directors of Signal and Miragen also considered other reasons for the Merger, as described herein. For example, Signal s board of directors considered, among other things:

- the strategic alternatives of Signal to the Merger, including potential transactions that could have resulted from discussions that Signal s management conducted with other potential merger parties;

- the consequences of current market conditions, Signal s current liquidity position, its depressed stock price and continuing net operating losses, and the likelihood that the resulting circumstances for the company would not change for the benefit of the Signal stockholders in the foreseeable future on a stand-alone basis;

- the risks of continuing to operate Signal on a stand-alone basis, including the need to continue building the company s tests services menu, infrastructure and management team to support the laboratory services business with insufficient capital resources;

- Signal management s belief that it would be difficult to obtain additional equity or debt financing on acceptable terms, if at all;

the opportunity as a result of the Merger for Signal stockholders to participate in the potential value that may result from development of the Miragen clinical development programs and the potential increase in value of the combined company following the Merger; and

the opinion of Cantor Fitzgerald & Co., referred to herein as Cantor, delivered to the board of directors of Signal (in its capacity as such) that, as of October 31, 2016 and based upon and subject to the assumptions made, procedures followed, matters considered, and qualifications and limitations set forth in the opinion, the Exchange Ratio for the conversion of Miragen capital stock into Signal common stock pursuant to the Merger Agreement was fair to Signal from a financial point of view.

In addition, Miragen s board of directors approved the Merger based on a number of factors, including the following:

the potential to provide its current stockholders with greater liquidity by owning stock in a public company;

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the potential to access of public market capital, including sources of capital from a broader range of investors to support the clinical development of its product candidates than it could otherwise obtain if it continued to operate as a privately-held company;

the expectation that the Merger would be a more time- and cost-effective means to access capital than other options considered, including an initial public offering;

the fact that shares of Signal common stock issued to Miragen stockholders will be registered pursuant to a registration statement on Form S-4 by Signal and will become freely tradable for Miragen s stockholders who are not affiliates of Miragen;

the likelihood that the Merger will be consummated on a timely basis;

the terms and conditions of the Merger Agreement, including, without limitation, the following:

the determination that the Exchange Ratio, which is not subject to adjustment based on trading prices, is appropriate to reflect the expected relative percentage ownership of Signal securityholders, Miragen securityholders and securityholders of those shares sold in the concurrent financing was appropriate in the judgment of Miragen s board of directors;

the expectation that the Merger will be treated as a reorganization for U.S. federal income tax purposes, with the result that the Miragen stockholders will not recognize taxable gain or loss for U.S. federal income tax purposes upon the exchange of Miragen common stock for Signal common stock pursuant to the Merger;

the rights of Miragen under the Merger Agreement to consider certain unsolicited competing proposals under certain circumstances should Miragen receive a superior proposal; and

the conclusion of Miragen s board of directors that the potential termination fee of $300,000 and/or expense reimbursements of up to $100,000, payable by Signal to Miragen and the circumstances when such fee may be payable, were reasonable.

Opinion of Signal Financial Advisor (see page 99)

On April 28, 2016, Signal engaged Cantor to act as Signal s financial advisor in connection with consideration of potential strategic alternatives for Signal. As part of this engagement, Signal s board of directors requested that Cantor evaluate the fairness, from a financial point of view, to Signal of the Exchange Ratio for the conversion of Miragen common stock into Signal common stock pursuant to the Merger Agreement. On October 31, 2016, at a meeting of Signal s board of directors, Cantor rendered its oral opinion to Signal s board of directors (in its capacity as such), which opinion was subsequently confirmed by delivery of a written opinion dated October 31, 2016, that, as of such date and based upon and subject to the assumptions made, procedures followed, matters considered, and qualifications

and limitations set forth in the opinion, the Exchange Ratio for the conversion of Miragen common stock into Signal common stock pursuant to the Merger Agreement was fair, from a financial point of view, to Signal, as more fully described below under the caption *The Merger Opinion of Signal Financial Advisor*.

The full text of the written opinion of Cantor, dated October 31, 2016, which sets forth, among other things, the assumptions made, procedures followed, matters considered and qualifications and limitations of the review undertaken in connection with such opinion, is attached as *Annex I*. Holders of Signal common stock are urged to read this opinion carefully and in its entirety. Cantor s opinion was provided for the sole benefit and use of Signal s board of directors (in its capacity as such) in connection with its consideration of the Merger and addresses only the fairness to Signal, from a financial point of view, of the Exchange Ratio for the conversion of Miragen common stock into Signal common stock pursuant to the Merger Agreement. It does not address any other aspects of the Merger and does not constitute a recommendation as to how holders of Signal common stock or Miragen common stock should vote or act

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in connection with the Merger. The Exchange Ratio was determined through negotiations between Signal and Miragen and not pursuant to any recommendation of Cantor. The summary of the opinion set forth in the section of this proxy statement/prospectus/information statement captioned *The Merger Opinion of Signal Financial Advisor* is qualified in its entirety by reference to the full text of the opinion.

Interests of Certain Directors, Officers and Affiliates of Signal and Miragen (see pages 105 and 108)

In considering the recommendation of Signal s board of directors with respect to issuing shares of Signal common stock pursuant to the Merger Agreement and the other matters to be acted upon by Signal stockholders at the Signal special meeting, Signal stockholders should be aware that certain members of Signal s board of directors and executive officers of Signal have interests in the Merger that may be different from, or in addition to, interests they have as Signal stockholders. For example, Signal has permitted the severance payments to be paid under the employment agreements with each of Samuel D. Riccitelli, Signal s president and chief executive officer, and Tamara A. Seymour, Signal s chief financial officer, to be paid in a lump sum payment instead of monthly installments over the applicable period. The employment of Mr. Riccitelli and Ms. Seymour are expected to terminate no later than the consummation of the Merger. Furthermore, Signal approved the payment of the remainder of bonuses to its executive officers based on their performance during the 2015 fiscal year, contingent upon the closing of the proposed Merger. In the event that Signal s compensation committee determines that funds are available to provide for the payment of incentive compensation bonus payment for the 2016 performance of Mr. Riccitelli and Ms. Seymour, Mr. Riccitelli and Ms. Seymour are eligible to receive an amount to be determined by the compensation committee. In addition, immediately prior to the execution of the Merger Agreement, Signal entered into an amendment to the Note, or the Note Amendment, with Bennett S. LeBow, a member of Signal s board of directors and Signal s largest stockholder. The Note Amendment allows for the conversion of the outstanding balance per the Note Amendment plus an additional 11% premium on the outstanding balance into shares of Signal common stock immediately prior to the effective time of the Merger at a conversion price equal to $5.39 per share, which was the closing price of Signal s common stock on The NASDAQ Capital Market as of the effective date of the Note Amendment. The conversion provision of the Note Amendment is subject to, among other things, approval by Signal stockholders and if the conversion of the Note into Signal common stock is not approved by the stockholders or if the Merger Agreement is terminated prior to the completion of the Merger, the outstanding balance of the Note will not be converted into Signal s common stock and will remain outstanding.

As of December 31, 2016, directors and executive officers of Signal owned or controlled 26% of the outstanding shares of Signal common stock. Signal directors and executive officers have entered into support agreements in connection with the Merger. The support agreements are discussed in greater detail in the section titled *Agreements Related to the Merger Support Agreements* in this proxy statement/prospectus/information statement.

In considering the recommendation of Miragen s board of directors with respect to consenting to the adoption of the Merger Agreement and the approval of the Merger and related transactions, Miragen s stockholders should be aware that certain members of the board of directors and executive officers of Miragen have interests in the Merger that may be different from, or in addition to, interests they have as Miragen stockholders. For example, some of Miragen s executive officers and directors have options to purchase shares of Miragen common stock that will each convert into an option to purchase shares of Signal common stock, and some of Miragen s directors and executive officers are expected to become directors and executive officers of the combined company upon the closing of the Merger. Specifically, William S. Marshall, Ph.D., Jason A. Leverone, Adam S. Levy and Paul D. Rubin, M.D., all currently executive officers of Miragen, are expected to become executive officers of the combined company upon the closing of the Merger, with Dr. Marshall serving as the president and chief executive officer, Mr. Leverone serving as chief financial officer, Mr. Levy serving as chief business officer and Dr. Rubin serving as executive vice president, research and development. Additionally, Bruce L. Booth, Ph.D., John W. Creecy, Thomas E. Hughes, Ph.D., Kyle A.

Lefkoff, Kevin Koch, Ph.D., William S. Marshall, Ph.D., all current directors of Miragen, and

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Joseph L. Turner, who will be designated to serve on the board of directors of the combined company following the completion of the Merger. Reza Halse, Ph.D., has informed Miragen that he will resign as a member of Miragen s board of directors immediately prior to the effectiveness of the Merger. Some of Miragen officers, directors and significant stockholders also entered into support agreements in connection with the Merger. The support agreements are discussed in greater detail in the section titled *Agreements Related to the Merger Support Agreements* beginning on page 143.

Management Following the Merger (see page 247)

Effective as of the closing of the Merger, Signal s executive officers are expected to be the current Miragen management team, including:

Name	Title
William S. Marshall, Ph.D.	President and Chief Executive Officer
Jason A. Leverone	Chief Financial Officer, Treasurer and Secretary
Adam S. Levy	Chief Business Officer
Paul D. Rubin, M.D.	Executive Vice President, Research and Development

Overview of the Merger Agreement and Agreements Related to the Merger Agreement

Merger Consideration and Exchange Ratio (see page 123)

Immediately prior to the effective time of the Merger, each share of Miragen preferred stock outstanding at such time will be converted into one share of Miragen common stock as determined in accordance with the Miragen certificate of incorporation then in effect. At the effective time of the Merger:

- each share of Miragen common stock outstanding immediately prior to the effective time of the Merger will automatically be converted into the right to receive a number of shares of Signal common stock at a rate equal to the Exchange Ratio, which is currently estimated to be approximately 0.6995, prior to giving effect to the reverse stock split, and within a range of 0.6995 to 0.0466, after giving effect to the reverse stock split;

- each warrant to purchase shares of Miragen capital stock outstanding and unexercised immediately prior to the effective time of the Merger will be assumed by Signal and will become a warrant to purchase shares of Signal common stock, with the number of shares and exercise price being adjusted by the Exchange Ratio, which is currently estimated to be approximately 0.6995, prior to giving effect to the reverse stock split, and within a range of 0.6995 to 0.0466, after giving effect to the reverse stock split; and

- each option to purchase shares of Miragen common stock outstanding and unexercised immediately prior to the effective time of the Merger will be assumed by Signal and will become an option to purchase shares of Signal common stock, with the number of shares and exercise price being adjusted by the Exchange Ratio, which is currently estimated to be approximately 0.6995, prior to giving effect to the reverse stock split, and within a range of 0.6995 to 0.0466, after giving effect to the reverse stock split.

Immediately after the Merger, Miragen securityholders will own approximately 96% of the fully-diluted common stock of the combined company, with Signal securityholders owning approximately 4% of the fully-diluted common stock of the combined company, which is subject to adjustment before closing and assuming that Miragen closes its concurrent financing immediately prior to the effective time of the Merger. If the concurrent financing does not close, then Miragen securityholders would own approximately 94% of the fully-diluted common stock of the combined company, with Signal securityholders owning approximately 6% of the fully-diluted common stock of the combined company. See the section titled *The Merger Agreement Merger Consideration and Exchange Ratio.*

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There will be no adjustment to the total number of shares of Signal common stock that Miragen stockholders will be entitled to receive for changes in the market price of Signal common stock. Accordingly, the market value of the shares of Signal common stock issued pursuant to the Merger will depend on the market value of the shares of Signal common stock at the time the Merger closes, and could vary significantly from the market value on the date of this proxy statement/prospectus/information statement.

Treatment of Signal Warrants and Stock Options (see page 114)

All warrants to purchase shares of Signal s common stock that are outstanding immediately prior to the effective time of the Merger will remain outstanding following the effective time of the Merger. All options to purchase shares of Signal common stock and restricted stock units that are not exercised or settled, as applicable, prior to the effective time will be cancelled and terminated upon the effectiveness of the Merger.

Treatment of Miragen Warrants and Stock Options (see page 135)

At the effective time of the Merger, each outstanding option and warrant, whether or not vested, to purchase shares of Miragen capital stock unexercised immediately prior to the effective time of the Merger will be converted into an option or warrant to purchase shares of Signal common stock. All rights with respect to each Miragen option or warrant will be assumed by Signal in accordance with its terms. Accordingly, from and after the effective time of the Merger each option or warrant assumed by Signal may be exercised solely for shares of Signal common stock.

The number of shares of Signal common stock subject to each outstanding Miragen option or warrant assumed by Signal will be determined by multiplying the number of shares of Miragen capital stock that were subject to such option or warrant (on an as-converted to common stock basis), as applicable, by the Exchange Ratio and rounding the resulting number down to the nearest whole number of shares of Signal common stock. The per share exercise price for the shares of Signal common stock issuable upon exercise of each Miragen option or warrant assumed by Signal will be determined by dividing the per share exercise price of Miragen capital stock subject to such option or warrant, as applicable, by the Exchange Ratio and rounding the resulting exercise price up to the nearest whole cent. Any restriction on the exercise of any option or warrant will continue in full force and effect and the term, exercisability, vesting schedule and other provisions of such option or warrant will otherwise remain unchanged.

Conditions to the Completion of the Merger (see page 137)

To complete the Merger, Signal stockholders must approve Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8, and 9. Additionally, the Miragen stockholders must approve the Merger and adopt the Merger Agreement. In addition to obtaining such stockholder approvals, each of the other closing conditions set forth in the Merger Agreement must be satisfied or waived.

Non-Solicitation (see page 132)

The Merger Agreement contains provisions prohibiting Signal and Miragen from seeking a competing transaction, subject to specified exceptions described in the Merger Agreement. Under these non-solicitation provisions, each of Signal and Miragen has agreed that neither it nor its subsidiaries, nor any of its officers, directors, employees, representatives, affiliates, advisors or agents will directly or indirectly:

solicit, initiate, respond to or take any action to facilitate or encourage any inquiries or the communication, making, submission or announcement of any competing proposal or take any action that could reasonably be expected to lead to a competing proposal;

enter into or participate in any discussions or negotiations with any person with respect to any competing proposal;

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furnish any information regarding such party to any person in connection with, in response to, relating to or for the purpose of assisting with or facilitating a competing proposal;

approve, endorse or recommend any competing proposal, subject to the terms and conditions in the Merger Agreement;

execute or enter into any letter of intent or similar document or any contract contemplating or otherwise relating to any competing proposal; or

grant any waiver or release under any confidentiality, standstill or similar agreement (other than to the other party).

Termination of the Merger Agreement (see page 139)

Either Signal or Miragen can terminate the Merger Agreement under certain circumstances, which would prevent the Merger from being consummated.

Termination Fee (see page 139)

The Merger Agreement provides that, upon termination of the Merger Agreement under specified circumstances, Signal may be required to pay Miragen a termination fee of $300,000 and/or up to $100,000 in expense reimbursements, or Miragen may be required to pay Signal a termination fee of $300,000 and/or up to $100,000 in expense reimbursements.

Subscription Agreement (see page 142)

On October 31, 2016, prior to the execution of the Merger Agreement, Miragen entered into a subscription agreement, or the Subscription Agreement, with certain current stockholders of Miragen and certain new investors in Miragen pursuant to which Miragen agreed to sell, and the purchasers listed therein agreed to purchase, shares of Miragen common stock for an aggregate purchase price of $40.7 million.

The consummation of the financing contemplated by the Subscription Agreement is subject to certain conditions, including the satisfaction or waiver of each of the conditions to the consummation of the Merger set forth in the Merger Agreement and the parties to the Merger Agreement being ready, willing and able to consummate the Merger immediately after the closing of the financing, which include (i) the SEC having declared effective the registration statement on Form S-4 of which this proxy statement/prospectus/information statement is a part and no stop order suspending the effectiveness of the registration statement on Form S-4 of which this proxy statement/prospectus/information statement is a part having been issued and remain pending, and (ii) the approval of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8, and 9 by Signal stockholders.

Support Agreements (see page 143)

In connection with the execution of the Merger Agreement, officers, directors and some stockholders of Miragen, who collectively beneficially own or control approximately 78% of the voting power of Miragen s outstanding capital stock on an as-converted to common stock basis as of December 31, 2016 entered into support agreements with Signal under which such stockholders have agreed to vote in favor of the Merger and the Merger Agreement and against any

competing transaction.

In connection with the execution of the Merger Agreement, Signal s officers, directors and some stockholders of Signal, who collectively beneficially own or control approximately 26% of Signal common stock as of December 31, 2016, also entered into support agreements with Miragen under which such stockholder has agreed to vote in favor of the Signal Proposals and against any competing transaction.

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Each stockholder executing a support agreement has made representations and warranties to Signal or Miragen, as applicable, regarding ownership and unencumbered title to the shares subject to such agreement, such stockholder s power and authority to execute the support agreement, due execution and enforceability of the support agreement, and ownership and unencumbered title to the shares. Unless otherwise waived, all of these support agreements prohibit the transfer, sale, assignment, gift or other disposition by the stockholder of their respective shares of Signal or Miragen capital stock, or the entrance into an agreement or commitment to do any of the foregoing, subject to specified exceptions. Each Miragen stockholder executing a support agreement has also waived its statutory appraisal rights in connection with the Merger.

The support agreements will terminate at the earlier of the effective time of the Merger or the termination of the Merger Agreement in accordance with its terms.

Lock-up Agreements (see page 144)

The officers, directors and certain other securityholders of Miragen also entered into lock-up agreements, pursuant to which such securityholders have agreed not to, except in limited circumstances, offer, pledge, sell, contract to sell, sell any option to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, any Miragen securities or shares of Signal common stock, including, as applicable, shares received in the Merger and issuable upon exercise of certain warrants and options, until 180 days after the closing date of the Merger.

The Miragen stockholders who have executed lock-up agreements as of December 31, 2016 owned, in the aggregate, approximately 98% of the shares of Miragen s outstanding capital stock on an as-converted to common stock basis.

Regulatory Approvals (see page 135)

In the United States, Signal must comply with applicable federal and state securities laws and the rules and regulations of The NASDAQ Capital Market in connection with the issuance of shares of Signal common stock and the filing of this proxy statement/prospectus/information statement with the SEC. As of the date hereof, the registration statement on Form S-4 of which this proxy statement/prospectus/information statement is a part has not become effective.

Material U.S. Federal Income Tax Consequences of the Merger (for more information, see page 115)

Each of Signal and Miragen intends the Merger to qualify as a reorganization within the meaning of Section 368(a) of the Code. In general, and subject to the qualifications and limitations set forth in the section titled *The Merger Material U.S. Federal Income Tax Consequences of the Merger*, if the Merger qualifies as a reorganization within the meaning of Section 368(a) of the Code, the material tax consequences to U.S. Holders of Miragen common stock will be as follows:

- a Miragen stockholder will not recognize gain or loss upon the exchange of Miragen common stock for Signal common stock pursuant to the Merger, except to the extent of cash received in lieu of a fractional share of Signal common stock as described below;

- a Miragen stockholder who receives cash in lieu of a fractional share of Signal common stock in the Merger will recognize capital gain or loss in an amount equal to the difference between the amount of cash received

in lieu of a fractional share and the stockholder s tax basis allocable to such fractional share;

a Miragen stockholder s aggregate tax basis for the shares of Signal common stock received in the Merger (including any fractional share interest for which cash is received) will equal the stockholder s aggregate tax basis in the shares of Miragen common stock surrendered in the Merger; and

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the holding period of the shares of Signal common stock received by a Miragen stockholder in the Merger will include the holding period of the shares of Miragen common stock surrendered in exchange therefor.

Tax matters are very complicated, and the tax consequences of the Merger to a particular Miragen stockholder will depend on such stockholder s circumstances. Accordingly, you are strongly urged to consult your tax advisor for a full understanding of the tax consequences of the Merger to you, including the applicability and effect of federal, state, local and non-U.S. income and other tax laws.

NASDAQ Stock Market Listing (see page 118)

Signal has filed an initial listing application for the combined company with The NASDAQ Capital Market. If such application is accepted, Signal anticipates that Signal s common stock will be listed on The NASDAQ Capital Market following the closing of the Merger under the trading symbol MGEN.

Anticipated Accounting Treatment (see page 118)

The Merger will be treated by Signal as a reverse merger under the acquisition method of accounting in accordance with accounting principles generally accepted in the United States, or U.S. GAAP. For accounting purposes, Miragen is considered to be acquiring Signal in the Merger.

Appraisal Rights and Dissenters Rights (see page 119)

Holders of Signal common stock are not entitled to appraisal rights in connection with the Merger. Holders of Miragen common stock are entitled to appraisal rights in connection with the Merger under Delaware law. For more information about such rights, see the provisions of Section 262 of the Delaware General Corporation Law, or the DGCL, attached hereto as *Annex J*, and the section titled *The Merger Appraisal Rights and Dissenters Rights* in this proxy statement/prospectus/information statement.

Comparison of Stockholder Rights (see page 288)

Both Signal and Miragen are incorporated under the laws of the State of Delaware and, accordingly, the rights of the stockholders of each are currently, and will continue to be, governed by the DGCL. If the Merger is completed, Miragen stockholders will become stockholders of Signal, and their rights will be governed by the DGCL, the bylaws of Signal and the certificate of incorporation of Signal, as may be amended by Signal Proposal Nos. 6, 7, 8, 9 and 10 if approved by Signal stockholders at the Signal special meeting. The rights of Signal stockholders contained in the certificate of incorporation, as amended, and bylaws of Signal differ from the rights of Miragen stockholders under the amended and restated certificate of incorporation and bylaws of Miragen, as more fully described under the section titled *Comparison of Rights of Holders of Signal Capital Stock and Miragen Capital Stock* in this proxy statement/prospectus/information statement.

Risk Factors (see page 19)

Both Signal and Miragen are subject to various risks associated with their businesses and their industries. In addition, the Merger, including the possibility that the Merger may not be completed, poses a number of risks to each company and its respective stockholders, including the following risks:

the Exchange Ratio is not adjustable based on the market price of Signal common stock so the Merger consideration at the closing may have a greater or lesser value than at the time the Merger Agreement was signed;

failure to complete the Merger may result in Signal or Miragen paying a termination fee to the other party and could harm the common stock price of Signal and future business and operations of each company;

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if the conditions to the Merger are not met, the Merger may not occur;

the Merger may be completed even though material adverse changes may result from the announcement of the Merger, industry-wide changes and other causes;

while Miragen has commitments for the sale of $40.7 million in shares of its common stock, consummation of this financing is not a condition to closing the Merger. If Miragen and Signal complete the Merger, but Miragen does not complete the concurrent financing, then the combined company may need to raise additional capital by issuing securities or debt or through licensing arrangements, which may be on worse commercial terms than the concurrent financing, cause significant dilution to the combined company s stockholders, restrict the combined company s operations or require the combined company to relinquish proprietary rights;

some Signal and Miragen executive officers and directors have interests in the Merger that are different from yours and that may influence them to support or approve the Merger without regard to your interests;

the market price of Signal common stock following the Merger may decline as a result of the Merger;

Miragen and Signal securityholders will have a reduced ownership and voting interest in, and will exercise less influence over the management of, the combined company as compared to their current ownership and voting interest in the respective companies following the completion of the Merger;

during the pendency of the Merger, Signal and Miragen may not be able to enter into a business combination with another party at a favorable price because of restrictions in the Merger Agreement, which could adversely affect their respective businesses;

certain provisions of the Merger Agreement may discourage third parties from submitting competing proposals, including proposals that may be superior to the arrangements contemplated by the Merger Agreement; and

because the lack of a public market for Miragen s capital stock makes it difficult to evaluate the fairness of the Merger, the stockholders of Miragen may receive consideration in the Merger that is less than the fair market value of Miragen s capital stock and/or Signal may pay more than the fair market value of Miragen s capital stock.

These risks and other risks are discussed in greater detail under the section titled *Risk Factors* in this proxy statement/prospectus/information statement. Signal and Miragen both encourage you to read and consider all of these risks carefully.

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SELECTED HISTORICAL AND UNAUDITED PRO FORMA

COMBINED FINANCIAL INFORMATION AND DATA

The following tables present summary historical financial data for Signal and Miragen, summary unaudited pro forma condensed combined financial data for Signal and Miragen, and comparative historical and unaudited pro forma per share data for Signal and Miragen.

Selected Historical Consolidated Financial Data of Signal

The selected consolidated statements of operations data for the years ended December 31, 2015 and 2014 and the selected consolidated balance sheet data as of December 31, 2015 and 2014 are derived from Signal s audited consolidated financial statements included elsewhere in this proxy statement/prospectus/information statement. The selected statements of operations data for the nine months ended September 30, 2016 and 2015 and the selected balance sheet data as of September 30, 2016 and 2015 are derived from Signal s unaudited interim financial statements included elsewhere in this proxy statement/prospectus/information statement. Signal s unaudited interim financial statements have been prepared in accordance with U.S. GAAP on the same basis as its audited annual consolidated financial statements and, in the opinion of management, reflect all adjustments, consisting only of normal, recurring adjustments, necessary for the fair presentation of those unaudited interim consolidated financial statements. Signal s historical results are not necessarily indicative of the results that may be expected in any future period and the results for the nine months ended September 30, 2016 are not necessarily indicative of results to be expected for the full year ending December 31, 2016 or any other period.

The selected historical consolidated financial data below should be read in conjunction with the sections titled *Signal Management s Discussion and Analysis of Financial Condition and Results of Operations*, *Risk Factors Risks Related to Signal* and Signal s consolidated financial statements and related notes included elsewhere in this proxy statement/prospectus/information statement.

	Years Ended December 31,		Nine Months Ended September 30,	
(in thousands, except share and per share data)	**2015**	**2014**	**2016**	**2015**
Consolidated statements of operations data				
Net revenue(1)	$ 2,538	$ 4,320	$ 2,581	$ 1,879
Operating expenses:				
Cost of revenue	2,472	3,366	1,856	2,016
Research and development	1,002	347	867	546
Selling and marketing	2,559	717	1,438	1,804
General and administrative	7,692	6,857	5,455	5,743
Gain on legal settlement		(100)		
Total operating expenses	13,725	11,187	9,616	10,109
Loss from operations	(11,187)	(6,867)	(7,035)	(8,230)
Interest expense	(141)	(1,023)	(69)	(118)

Net loss attributable to stockholders of Signal Genetics, Inc./members of Signal Genetics LLC	$ (11,328)	$ (7,890)	$ (7,104)	$ (8,348)
Net loss per common share, basic and diluted(2)	$ (21.00)	$ (52.50)	$ (9.90)	$ (17.25)
Weighted-average number of shares outstanding, basic and diluted(2)	539,460	150,390	716,957	482,308

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	As of December 31,		As of September 30,	
	2015	2014	2016	2015
Consolidated balance sheet data				
Cash and cash equivalents	$ 10,832	$ 5,119	$ 5,351	$ 12,124
Total assets	12,902	8,089	7,541	14,797
Note payable related party	1,105		1,105	1,105
Total liabilities	2,492	2,098	2,855	2,164
Total stockholders equity	10,410	5,991	4,686	12,633

(1) During the year ended December 31, 2015, net unfavorable changes in estimates were recorded to revenue related to non-contracted revenues recorded in the prior year of $193,000. During the year ended December 31, 2014, net unfavorable changes in estimates were recorded to revenue related to non-contracted revenues recorded in prior years of $380,000, of which $106,000 and $274,000 related to revenues previously recorded during 2012 and 2013, respectively.

(2) On November 4, 2016, Signal effected a one-for-15 reverse stock split of shares of its common stock. Share and per share amounts in the Selected Historical Financial Data of Signal reflect this reverse stock split of Signal common stock.

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Selected Historical Consolidated Financial Data of Miragen

The selected consolidated statements of operations data for the years ended December 31, 2015 and 2014 and the selected consolidated balance sheet data as of December 31, 2015 and 2014 are derived from Miragen s audited consolidated financial statements included elsewhere in this proxy statement/prospectus/information statement. The selected consolidated statements of operations data for the nine months ended September 30, 2016 and 2015 and the selected consolidated balance sheet data as of September 30, 2016 are derived from Miragen s unaudited interim condensed consolidated financial statements included elsewhere in this proxy statement/prospectus/information statement. Miragen s unaudited interim condensed consolidated financial statements have been prepared in accordance with U.S. GAAP on the same basis as its audited annual consolidated financial statements and, in the opinion of management, reflect all adjustments, consisting only of normal, recurring adjustments, necessary for the fair presentation of those unaudited interim condensed consolidated financial statements. Miragen s historical results are not necessarily indicative of the results that may be expected in any future period and the results for the nine months ended September 30, 2016 are not necessarily indicative of results to be expected for the full year ending December 31, 2016 or any other period.

The selected historical consolidated financial data below should be read in conjunction with the sections titled *Miragen Management s Discussion and Analysis of Financial Condition and Results of Operations*, *Risk Factors Risks Related to Miragen s Financial Condition and Capital Requirements* and Miragen s consolidated financial statements and related notes included elsewhere in this proxy statement/prospectus/information statement.

	Years Ended December 31,		Nine Months Ended September 30,	
(in thousands, except per share and share amounts)	**2015**	**2014**	**2016**	**2015**
Consolidated Statements of Operations Data:				
Revenue	$ 5,004	$ 7,641	$ 2,969	$ 4,016
Operating expenses:				
Research and development	13,312	9,488	9,786	9,918
General and administrative	3,850	4,068	4,255	2,902
Total operating expenses	17,162	13,566	14,041	12,820
Loss from operations	(12,158)	(5,915)	(11,072)	(8,804)
Interest and other income (expense), net	(3,528)	9	(229)	(1,599)
Net loss	$ (15,686)	$ (5,906)	$ (11,301)	$ (10,403)
Accretion of preferred stock to redemption value	(34)	(30)	(36)	(24)
Net loss applicable to common stockholders	$ (15,720)	$ (5,936)	$ (11,337)	$ (10,427)
Net loss per share, basic and diluted	$ (18.37)	$ (7.03)	$ (13.25)	$ (12.18)
Shares used in computing net loss per share, basic and diluted	855,734	844,093	855,734	855,734

	As of December 31,

(in thousands)	**2015**	**2014**	**As of September 30, 2016**
Consolidated Balance Sheet Data:			
Cash and cash equivalents	$ 21,235	$ 5,114	$ 24,598
Short term investments			1,001
Working capital	19,251	3,073	22,808
Total assets	23,536	7,119	28,434
Notes payable	4,934		5,098
Redeemable convertible preferred stock	60,850	36,057	76,967
Accumulated deficit	(49,753)	(34,033)	(61,090)
Total stockholders deficit	(45,290)	(32,822)	(56,498)

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Selected Unaudited Pro Forma Condensed Combined Financial Data of Signal and Miragen

The following information gives effect to Signal s one-for-15 reverse stock split of its common stock, which was effective at 5:01 p.m. Eastern Time on November 4, 2016, but does not give effect to the proposed reverse stock split described in Signal Proposal No. 7, beginning on page 167 in this proxy statement/prospectus/information statement.

(in thousands except per share amount)	Year Ended December 31, 2015	Nine Months Ended September 30, 2016
Unaudited Pro Forma Combined Consolidated Statements of Operations Data:		
Revenue	$ 5,004	$ 2,969
Operating expenses:		
Research and development	13,312	9,786
General and administrative	10,249	7,706
Total operating expenses	23,561	17,492
Loss from operations	(18,557)	(14,523)
Interest and other income (expense), net	(3,493)	(230)
Net loss	$ (22,050)	$ (14,753)
Net loss applicable to common stockholders	$ (22,050)	$ (14,753)
Net loss per share, basic and diluted	$ (1.26)	$ (0.71)
Shares used in computing net loss per share, basic and diluted	17,432,318	20,873,519

(in thousands)	As of September 30, 2016
Unaudited Pro Forma Combined Balance Sheet data:	
Consolidated Balance Sheet Data:	
Cash and cash equivalents	$ 70,197
Short term investments	1,001
Working capital	64,204
Total assets	74,317
Notes payable	5,098
Accumulated deficit	(61,503)
Total stockholders equity	61,929

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Comparative Historical and Unaudited Pro Forma Per Share Data

The following information gives effect to Signal s one-for-15 reverse stock split of its common stock, which was effective at 5:01 p.m. Eastern Time on November 4, 2016, but does not give effect to the proposed reverse stock split described in Signal Proposal No. 7, beginning on page 167 in this proxy statement/prospectus/information statement.

The information below reflects the historical net loss and book value per share of Signal common stock and the historical net loss and book value per share of Miragen common stock in comparison with the unaudited pro forma net loss and book value per share after giving effect to the Merger of Signal with Miragen on a pro forma basis.

You should read the tables below in conjunction with the audited and unaudited consolidated financial statements of Signal included in this proxy statement/prospectus/information statement and the audited and unaudited consolidated financial statements of Miragen included in this proxy statement/prospectus/information statement and the related notes and the unaudited pro forma condensed combined financial information and notes related to such financial statements included elsewhere in this proxy statement/prospectus/information statement.

	Nine Months Ended September 30, 2016	Year Ended December 31, 2015
Signal Historical Per Common Share Data:		
Basic and diluted net loss per share	$ (9.90)	$ (21.00)
Book value per share	6.51	14.68
Miragen Historical Per Common Share Data:		
Basic and diluted net loss per share	$ (13.25)	$ (18.37)
Book value per share	(66.02)	(52.93)
Signal and Miragen Combined Company Pro Forma Data:		
Basic and diluted net loss per share	$ (0.70)	$ (1.28)
Book value per share	2.95	N/A

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MARKET PRICE AND DIVIDEND INFORMATION

Signal common stock is listed on The NASDAQ Capital Market under the symbol SGNL. The following table presents, for the periods indicated, the range of high and low per share sales prices for Signal common stock as reported on The NASDAQ Capital Market for each of the periods set forth below. Miragen is a private company and its common stock and preferred stock are not publicly traded. These per share sales prices have not been adjusted to give effect to the proposed reverse stock split of Signal common stock.

Signal Common Stock

	High	Low
2014:		
Second Quarter (from June 18, 2014)	$ 149.84	$ 105.74
Third Quarter	$ 135.74	$ 61.80
Fourth Quarter	$ 75.00	$ 31.65
2015:		
First Quarter	$ 59.55	$ 26.40
Second Quarter	$ 44.10	$ 21.30
Third Quarter	$ 40.95	$ 13.20
Fourth Quarter	$ 18.60	$ 9.94
2016:		
First Quarter	$ 12.45	$ 6.15
Second Quarter	$ 11.10	$ 6.00
Third Quarter	$ 9.45	$ 6.00
Fourth Quarter	$ 15.11	$ 1.80

The closing price of Signal common stock on October 31, 2016, the last trading day prior to the public announcement of the Merger, was $5.39 per share and the closing price of Signal common stock on January 5, 2017 was $5.33 per share, in each case as reported on The NASDAQ Capital Market.

Because the market price of Signal common stock is subject to fluctuation, the market value of the shares of Signal common stock that Miragen stockholders will be entitled to receive in the Merger may increase or decrease.

Assuming approval of Signal Proposal No. 6 and successful application for initial listing with The NASDAQ Capital Market, following the completion of the Merger, Signal common stock will be listed on The NASDAQ Capital Market and will trade under Signal s new name, Miragen Therapeutics, Inc., and new trading symbol, MGEN.

As of December 31, 2016 Signal had 22 holders of record of its common stock. For detailed information regarding the beneficial ownership of some stockholders of Signal and Miragen, see the section titled *Principal Stockholders of Signal* beginning on page 297 and the section titled *Principal Stockholders of Miragen* beginning on page 299 of this proxy statement/prospectus/information statement.

Dividends

Signal has never paid or declared any cash dividends on its common stock and does not anticipate paying cash dividends on its common stock for the foreseeable future. Notwithstanding the foregoing, any determination to pay cash dividends subsequent to the Merger will be at the discretion of Signal s then-current board of directors

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and will depend upon a number of factors, including its results of operations, financial condition, future prospects, contractual restrictions, restrictions imposed by applicable law and other factors Signal s then-current board of directors deems relevant.

Miragen has never paid or declared any cash dividends on its common or preferred stock. If the Merger does not occur, Miragen does not anticipate paying any cash dividends on its common or preferred stock in the foreseeable future, and Miragen intends to retain all available funds and any future earnings to fund the development and expansion of its business. Any future determination to pay dividends will be at the discretion of Miragen s board of directors and will depend upon a number of factors, including its results of operations, financial condition, future prospects, contractual restrictions, restrictions imposed by applicable law and other factors Miragen s then-current board of directors deems relevant.

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RISK FACTORS

The combined company will be faced with a market environment that cannot be predicted and that involves significant risks, many of which will be beyond its control. In addition to the other information contained in this proxy statement/prospectus/information statement, you should carefully consider the material risks described below before deciding how to vote your shares of stock. In addition, you should read and consider the risks associated with the business of Signal because these risks may also affect the combined company these risks can be found in Signal s Annual Report on Form 10-K, as updated by subsequent Quarterly Reports on Form 10-Q, all of which are filed with the SEC. You should also read and consider the other information in this proxy statement/prospectus/information statement. Please see the section titled Where You Can Find More Information in this proxy statement/prospectus/information statement.

Risks Related to the Merger

The Exchange Ratio is not adjustable based on the market price of Signal common stock so the Merger consideration at the closing may have a greater or lesser value than at the time the Merger Agreement was signed.

It is currently anticipated that, at the closing of the Merger, the Exchange Ratio would be approximately 0.6995 pre-split shares of Signal common stock and would be within a range of approximately 0.6995 and 0.0466 post-split shares of Signal common stock. These estimates are subject to adjustment prior to closing of the Merger, including (i) adjustments to account for the issuance of any additional shares of Miragen or Signal common stock, as applicable, prior to the consummation of the Merger, provided that, the issuance of Miragen common stock in the concurrent financing will not impact the Exchange Ratio, or (ii) an upward adjustment to the extent that Signal s net cash at the effective time of the Merger is less than negative $100,000 (and as a result, Signal securityholders could own less, and Miragen securityholders could own more, of the combined company). Any changes in the market price of Signal common stock before the completion of the Merger will not affect the number of shares Miragen securityholders will be entitled to receive pursuant to the Merger Agreement. Therefore, if before the completion of the Merger the market price of Signal common stock declines from the market price on the date of the Merger Agreement, then Miragen securityholders could receive Merger consideration with substantially lower value. Similarly, if before the completion of the Merger the market price of Signal common stock increases from the market price on the date of the Merger Agreement, then Miragen securityholders could receive Merger consideration with substantially more value for their shares of Miragen capital stock than the parties had negotiated for in the establishment of the Exchange Ratio. The Merger Agreement does not include a price-based termination right. However, Miragen s obligation to consummate the Merger is conditioned upon Signal having Net Cash that is greater than or equal to negative $300,000, as defined and described under *The Merger Agreement Conditions to the Completion of the Merger*. Because the Exchange Ratio does not adjust as a result of changes in the value of Signal common stock, for each one percentage point that the market value of Signal common stock rises or declines, there is a corresponding one percentage point rise or decline, respectively, in the value of the total Merger consideration issued to Miragen securityholders.

Failure to complete the Merger may result in Signal or Miragen paying a termination fee to the other party and could harm the common stock price of Signal and future business and operations of each company.

If the Merger is not completed, Signal and Miragen are subject to the following risks:

- if the Merger Agreement is terminated under specified circumstances, Signal or Miragen will be required to pay the other party a termination fee of $300,000 and/or up to $100,000 in expense reimbursements;

the price of Signal common stock may decline and remain volatile;

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costs related to the Merger, such as legal and accounting fees, which Signal and Miragen estimate will total approximately $800,000 and $1.1 million, respectively, some of which must be paid even if the Merger is not completed; and

Signal may be forced to cease its operations, dissolve and liquidate its assets.

In addition, if the Merger Agreement is terminated and the board of directors of Signal or Miragen determines to seek another business combination, there can be no assurance that either Signal or Miragen will be able to find a partner willing to provide equivalent or more attractive consideration than the consideration to be provided by each party in the Merger.

If the conditions to the Merger are not met, the Merger may not occur.

Even if the Merger is approved by the stockholders of Miragen and change of control and related share issuance are approved by the stockholders of Signal, specified conditions must be satisfied or waived to complete the Merger. These conditions are set forth in the Merger Agreement and described in the section titled *The Merger Agreement Conditions to the Completion of the Merger* in this proxy statement/prospectus/information statement. Signal and Miragen cannot assure you that all of the conditions will be satisfied or waived. If the conditions are not satisfied or waived, the Merger may not occur or will be delayed, and Signal and Miragen each may lose some or all of the intended benefits of the Merger.

The Merger may be completed even though material adverse changes may result from the announcement of the Merger, industry-wide changes and other causes.

In general, either Signal or Miragen can refuse to complete the Merger if there is a material adverse change affecting the other party between October 31, 2016, the date of the Merger Agreement, and the closing of the Merger. However, certain types of changes do not permit either party to refuse to complete the Merger, even if such change could be said to have a material adverse effect on Signal or Miragen, including:

any effect, change, event, circumstance or development in the conditions generally affecting the industries in which Miragen and Signal operate or the U.S. or global economy or capital markets as a whole;

the failure by Miragen to complete the concurrent financing in connection with the Merger;

any natural disaster or any acts of terrorism, sabotage, military action or war or any escalation of worsening thereof;

any change in accounting requirements or principles or any change in applicable laws, rules or regulations or the interpretation thereof;

any effect resulting from the announcement or pendency of the Merger or any related transactions;

any failure by Signal or Miragen to meet internal projections or forecasts or third-party revenue or earnings predictions for any period ending on or after October 31, 2016;

with respect to Signal, any change in the price or trading volume of Signal common stock;

any rejection by a governmental body of a registration or filing by Miragen or Signal relating to specified intellectual property rights; or

with respect to Miragen, any change in the cash position of Miragen which results from operations in the ordinary course of business.

If adverse changes occur and Signal and Miragen still complete the Merger, the stock price of the combined company may suffer. This in turn may reduce the value of the Merger to the stockholders of Signal, Miragen or both.

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While Miragen has commitments for the sale of $40.7 million in shares of its common stock, consummation of this financing is not a condition to closing the Merger. If Miragen and Signal complete the Merger, but Miragen does not complete the concurrent financing, then the combined company may need to raise additional capital by issuing securities or debt or through licensing arrangements, which may be on worse commercial terms than the concurrent financing, cause significant dilution to the combined company s stockholders, restrict the combined company s operations or require the combined company to relinquish proprietary rights.

Since the concurrent financing is not a condition to the Merger, Miragen and Signal may complete the Merger, but Miragen may not complete the concurrent financing. If this were to occur, the combined company would have substantially less funds than Miragen and Signal currently anticipate and may be required to raise additional funds sooner than currently planned. Additional financing may not be available to the combined company when it needs it or may not be available on favorable terms. To the extent that the combined company raises additional capital by issuing equity securities, the terms of such an issuance may be on worse commercial terms than the concurrent financing and may cause more significant dilution to the combined company s stockholders ownership. and the terms of any new equity securities may have preferences over the combined company s common stock. Any debt financing the combined company enters into may involve covenants that restrict its operations. These restrictive covenants may include limitations on additional borrowing and specific restrictions on the use of the combined company s assets, as well as prohibitions on its ability to create liens, pay dividends, redeem its stock or make investments. In addition, if the combined company raises additional funds through licensing arrangements, it may be necessary to relinquish potentially valuable rights to current product candidates and potential products or proprietary technologies, or grant licenses on terms that are not favorable to the combined company.

Some Signal and Miragen executive officers and directors have interests in the Merger that are different from yours and that may influence them to support or approve the Merger without regard to your interests.

Some officers and directors of Signal and Miragen participate in arrangements that provide them with interests in the Merger that are different from yours, including, among others, the continued service as an officer or director of the combined company, severance and retention benefits, the acceleration of stock option and restricted stock vesting, payment of deferred and current year incentive compensation, additional premiums associated with outstanding indebtedness, continued indemnification and the potential ability to sell an increased number of shares of common stock of the combined company in accordance with Rule 144 under the Securities Act of 1933, as amended, or the Securities Act. For more information regarding the interests of the Signal and Miragen executive officers and directors in the Merger, see the sections titled *The Merger Interests of the Signal Directors and Executive Officers in the Merger* and *The Merger Interests of Miragen Directors and Executive Officers in the Merger* of this proxy statement/prospectus/information statement.

The market price of Signal common stock following the Merger may decline as a result of the Merger.

The market price of Signal common stock may decline as a result of the Merger for a number of reasons, including if:

- investors react negatively to the prospects of the combined company s business and prospects from the Merger;
- the effect of the Merger on the combined company s business and prospects is not consistent with the expectations of financial or industry analysts; or

the combined company does not achieve the perceived benefits of the Merger as rapidly or to the extent anticipated by financial or industry analysts.

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Miragen and Signal securityholders will have a reduced ownership and voting interest in, and will exercise less influence over the management of, the combined company as compared to their current ownership and voting interest in the respective companies following the completion of the Merger.

After the completion of the Merger, the current stockholders of Miragen and Signal will own a smaller percentage of the combined company than their ownership of their respective companies prior to the Merger. Immediately after the Merger, Miragen securityholders will own approximately 96% of the fully-diluted common stock of Signal, with Signal securityholders, whose shares of Signal common stock will remain outstanding after the Merger, owning approximately 4% of the fully-diluted common stock of the combined company, each assuming that Miragen closes its concurrent financing immediately prior to the effective time of the Merger. If the concurrent financing does not close, then Miragen s securityholders would own approximately 94% of the fully-diluted common stock of the combined company and Signal s securityholders would own approximately 6% of the fully-diluted common stock of the combined company. These estimates are based on the anticipated pre-split Exchange Ratio and post-split Exchange Ratios and are subject to adjustment. In addition, the seven-member board of directors of the combined company will initially consist of William S. Marshall, Ph.D., Bruce L. Booth, Ph.D., John W. Creecy, Thomas E. Hughes, Ph.D., Kevin Koch, Ph.D., Kyle A. Lefkoff and Joseph L. Turner. Consequently, securityholders of Miragen and Signal will be able to exercise less influence over the management and policies of the combined company than they currently exercise over the management and policies of their respective companies.

During the pendency of the Merger, Signal and Miragen may not be able to enter into a business combination with another party at a favorable price because of restrictions in the Merger Agreement, which could adversely affect their respective businesses.

Covenants in the Merger Agreement impede the ability of Signal and Miragen to make acquisitions, subject to specified exceptions relating to fiduciary duties or complete other transactions that are not in the ordinary course of business pending completion of the Merger. As a result, if the Merger is not completed, the parties may be at a disadvantage to their competitors during that period. In addition, while the Merger Agreement is in effect, each party is generally prohibited from soliciting, initiating, encouraging or entering into specified extraordinary transactions, such as a Merger, sale of assets or other business combination, with any third party, subject to specified exceptions. Any such transactions could be favorable to such party s stockholders.

Certain provisions of the Merger Agreement may discourage third parties from submitting competing proposals, including proposals that may be superior to the arrangements contemplated by the Merger Agreement.

The terms of the Merger Agreement prohibit each of Signal and Miragen from soliciting competing proposals or cooperating with persons making unsolicited takeover proposals, except in limited circumstances when such party s board of directors determines in good faith, after consultation with its independent financial advisor, if any, and outside counsel, that an unsolicited competing proposal constitutes, or would reasonably be expected to result in, a superior competing proposal and that failure to take such action would be reasonably likely to result in a breach of the fiduciary duties of the board of directors. In addition, if Signal or Miragen terminate the Merger Agreement under specified circumstances, including terminating because of a decision of a board of directors to recommend a superior competing proposal, Signal or Miragen would be required to pay a termination fee of $300,000 and/or up to $100,000 in expense reimbursements to the other party. If the Merger Agreement is terminated under specified circumstances, Signal or Miragen will be required to pay the other party a termination fee of $300,000, and/or up to $100,000 in expense reimbursements, as defined and described under *The Merger Agreement Termination of the Merger Agreement and Termination Fee.* This termination fee may discourage third parties from submitting competing proposals to Signal or Miragen or their stockholders, and may cause the respective boards of directors to be less inclined to recommend a competing proposal.

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Because the lack of a public market for Miragen s capital stock makes it difficult to evaluate the fairness of the Merger, the stockholders of Miragen may receive consideration in the Merger that is less than the fair market value of Miragen s capital stock and/or Signal may pay more than the fair market value of Miragen s capital stock

The outstanding capital stock of Miragen is privately held and is not traded in any public market. The lack of a public market makes it extremely difficult to determine the fair market value of Miragen s capital stock. Because the percentage of Signal equity to be issued to Miragen stockholders was determined based on negotiations between the parties, it is possible that the value of the Signal common stock to be received by Miragen stockholders will be less than the fair market value of Miragen s capital stock, or Signal may pay more than the aggregate fair market value for Miragen s capital stock.

Risks Related to Signal

Signal is an early stage company with a limited commercial history and a history of net losses; Signal expects to incur net losses in the future and may never achieve sustained profitability.

Signal is a diagnostics company with a limited commercial history. Substantially all of Signal s revenue has been derived from its MyPRS testing services, which was launched in 2011. Signal has historically incurred substantial net losses. Signal incurred losses attributable to stockholders of Signal Genetics, Inc. (or members of Signal Genetics LLC, as applicable) of $11.3 million and $7.9 million during the years ended December 31, 2015 and 2014, respectively. As of September 30, 2016, Signal had cash and cash equivalents totaling $5.4 million. Signal s existing cash resources will not be sufficient to meet its operating plan for the full 12-month period after the date of this proxy statement/prospectus/information statement. Based on available resources, Signal believes it can maintain its operations into the second quarter of 2017. Signal expects its losses to continue as a result of ongoing research and development expenses, increased selling and marketing costs and increased general and administrative costs to support Signal s planned growth. These losses have had, and will continue to have, an adverse effect on Signal s working capital, total assets and stockholders equity. Because of the numerous risks and uncertainties associated with Signal s research, development and commercialization efforts, Signal is unable to predict when it will become profitable, and Signal may never become profitable. Even if Signal does achieve profitability, it may not be able to sustain or increase profitability on a quarterly or annual basis. Signal s inability to achieve and then maintain profitability would negatively affect its business, financial condition, results of operations and cash flows.

If the Merger is not completed, Signal would need to raise substantial additional funding to the extent it continues its commercialization and research and development efforts, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force Signal to dissolve or liquidate its operations.

Signal s operations have consumed substantial amounts of cash since inception. As of September 30, 2016, Signal s cash, cash equivalents and investments were approximately $5.4 million. Signal s total operating expenses were $9.6 million and $10.1 million for the nine months ended September 30, 2016 and 2015, respectively. Signal believes that its existing cash, cash equivalents and investments will enable it to fund its operations into the second quarter of 2017. However, Signal has historically incurred substantial net losses and maintaining and growing revenues from MyPRS depends on the availability of adequate coverage and reimbursement for Signal s tests from third-party payors, including government programs such as Medicare, private insurance plans and managed care programs. Therefore, Signal will need to raise substantial additional capital to fund future activities.

Any additional fundraising efforts may divert Signal s management from their day-to-day activities, which may adversely affect its ability to develop and commercialize additional diagnostic tests. In addition, it cannot guarantee

that future financing will be available in sufficient amounts or on terms acceptable to Signal, if at all. If Signal is unable to obtain funding on a timely basis, it may be required to significantly curtail or be unable to

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deploy the capital necessary to refocus or expand its operations or otherwise capitalize on its business opportunities, as desired, any of which could materially adversely affect its business, financial condition and results of operations and could even require it to cease operations entirely.

If the Merger is not completed, raising additional funds through debt or equity financing is likely to be difficult, could be dilutive and may cause the market price of Signal s common stock to decline further.

To the extent that Signal raises additional capital through the sale of equity or convertible debt securities, the issuance of those securities could result in substantial dilution for Signal s current stockholders and the terms may include liquidation or other preferences that adversely affect the rights of its current stockholders. Furthermore, the issuance of additional securities, whether equity or debt, by Signal, or the possibility of such issuance, may cause the market price of its common stock to decline further and existing stockholders may not agree with its financing plans or the terms of such financings.

If the Merger is not completed, Signal will require, and may not be able to obtain, substantial additional financial resources in order to carry out planned activities and to continue as a going concern beyond the second quarter of 2017.

As of September 30, 2016, Signal has cash and cash equivalents totaling $5.4 million. Signal s existing cash resources will not be sufficient to meet its operating plan for the full 12-month period after the date of this proxy statement/prospectus/information statement. Based on available resources, Signal believes it can maintain its operations into the second quarter of 2017. As a result, to continue to fund Signal s operations beyond the second quarter of 2017, Signal would need to (i) raise additional capital through the issuance of equity, debt or other securities, (ii) convert its existing debt into equity, (iii) enter into strategic partnerships, alliances, collaborations or other similar transactions or (iv) a combination thereof. Due to current market conditions, Signal s current liquidity position and its stock price, Signal believes it may be difficult to obtain additional equity or debt financing on terms acceptable to Signal, if at all, thus raising substantial doubt about Signal s ability to continue as a going concern. If Signal is unable to raise additional capital or successfully complete the Merger or another strategic partnership, alliance, collaboration or other similar transaction, Signal will need to delay or reduce expenses or limit or curtail operations, any of which would have a material adverse effect on its business. Further, if Signal is unable to raise additional capital or successfully complete the Merger or a strategic partnership, alliance, collaboration or other similar transaction on a timely basis and on terms that are acceptable, Signal may also be required to sell or license its assets, sell the company or otherwise liquidate all or a portion of Signal s assets and/or cease its operations altogether. If Signal cannot continue as a viable entity, its stockholders might lose some or all of their investment. Signal s financial statements do not include any adjustments that might be necessary if Signal is unable to continue as a going concern.

Signal s business to date has been almost entirely dependent on the success of MyPRS, and a small number of test ordering sites account for most of the sales of Signal s tests and services.

Due to the early stage nature of Signal s business and its limited selling and marketing activities to date, Signal has historically derived a significant portion of Signal s revenue from a limited number of test ordering sites. In particular, the most significant portion of Signal s revenue is generated from its MyPRS test services provided at its clinical laboratory in Little Rock, Arkansas for three major customers, including UAMS. Revenue sourced either from or through UAMS as a percentage of net revenue during the first nine months of 2016 and 2015 were 22% and 64%, respectively. The decrease in revenue is due to the decrease in research funds available at UAMS for such programs. Signal expects continued declining revenue from the UAMS research programs. Signal s test ordering sites are largely hospitals and cancer centers. Oncologists and pathologists at these sites order the tests on behalf of their oncology

patients or as part of a clinical trial sponsored by a pharmaceutical company in which the patient is enrolled. Signal generally does not enter into formal written agreements with such test ordering sites and, as a result, Signal may lose the business of any of these test ordering sites at any time.

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Signal has suspended certain activities to reduce operating expenses while seeking a merger or sale. There can be no assurance that the proposed Merger transaction will be approved or consummated, or if consummated, that it would enhance stockholder value. If the Merger is not consummated, there also can be no assurance that Signal can increase its revenue.

There is no assurance that the proposed Merger between Signal and Miragen will be completed in a timely manner or at all. If the Merger with Miragen is not consummated, Signal s business could suffer materially and its stock price could decline.

The consummation of the proposed Merger between Signal and Miragen is subject to a number of closing conditions, including the approval by Signal stockholders and other customary closing conditions. The parties are targeting a closing of the transaction in the first quarter of 2017, however, there can be no assurance that the proposed Merger will be consummated on their desired timeframe, or at all.

If the proposed Merger between Signal and Miragen is not consummated, Signal may be subject to a number of material risks, and its business and stock price could be adversely affected, as follows:

- Signal has incurred and expects to continue to incur significant expenses related to the proposed Merger with Miragen even if the Merger is not consummated;
- Signal could be obligated to pay Miragen a $300,000 termination fee and/or up to $100,000 in expense reimbursements in connection with the termination of the Merger Agreement, depending on the reason for the termination;
- The market price of Signal s common stock may decline to the extent that the current market price reflects a market assumption that the proposed Merger will be completed; and
- If the sale of the MyPRS intellectual property assets is approved by the stockholders of Signal or as a result of limited financial resources, Signal may not pursue an alternate merger transaction if the proposed Merger with Miragen is not completed.

If the Merger is not completed, Signal s board of directors may decide to pursue a dissolution and liquidation of the company. In such an event, the amount of cash available for distribution to its stockholders will depend heavily on the timing of such liquidation as well as the amount of cash that will need to be reserved for commitments and contingent liabilities.

There can be no assurance that the Merger will be completed. If the Merger is not completed, Signal s board of directors may decide to pursue a dissolution and liquidation of the company. In such an event, the amount of cash available for distribution to its stockholders will depend heavily on the timing of such decision, as with the passage of time the amount of cash available for distribution will be reduced as Signal continues to fund its operations. In addition, if Signal s board of directors were to approve and recommend, and its stockholders were to approve, a dissolution and liquidation of the company, it would be required under Delaware corporate law to pay its outstanding obligations, as well as to make reasonable provision for contingent and unknown obligations, prior to making any distributions in liquidation to its stockholders. Signal s commitments and contingent liabilities may include

(i) non-cancelable lease obligations and (ii) non-cancellable operating expenses associated with winding down operations. As a result of this requirement, a portion of Signal s assets may need to be reserved pending the resolution of such obligations. In addition, Signal may be subject to litigation or other claims related to a dissolution and liquidation of its company. If a dissolution and liquidation were pursued, Signal s board of directors, in consultation with its advisors, would need to evaluate these matters and make a determination about a reasonable amount to reserve. Accordingly, holders of its common stock could lose all or a significant portion of their investment in the event of Signal s liquidation, dissolution or winding up.

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If Signal fails to continue to meet all applicable NASDAQ Capital Market requirements and NASDAQ determines to delist Signal s common stock, the delisting could adversely affect the value of the Merger, market liquidity of its common stock and the market price of its common stock could decrease.

Signal s common stock is listed on The NASDAQ Capital Market. In order to maintain the listing, Signal must meet minimum financial and other requirements, including requirements for a minimum amount of capital, a minimum price per share and continued business operations so that it is not characterized as a public shell company. If Signal is unable to comply with NASDAQ s listing standards, NASDAQ may determine to delist its common stock from The NASDAQ Capital Market. If its common stock is delisted for any reason, it could reduce the value of its common stock and its liquidity. Delisting could also adversely affect the ability to obtain financing for the continuation of Signal s operations, if Signal chooses to reestablish its business, or to use its common stock in acquisitions, including the Merger. Delisting could result in the loss of confidence by suppliers and employees. Delisting would prevent Signal from satisfying a closing condition for the Merger, and, in such event, Miragen may elect not to consummate the Merger. In addition, the combined company must submit a new application for listing on NASDAQ after the Merger pursuant to the reverse merger rules, and the combined company will need to meet NASDAQ s minimum listing requirements condition.

If Signal is unable to complete the sale of the MyPRS intellectual property assets and receive the anticipated cash proceeds from the sale as planned, then Signal may have incurred additional expenses that may not allow Signal to satisfy the closing net cash requirement contained in the Merger Agreement.

The Merger Agreement contains a condition precedent to the obligation of Miragen to complete the Merger, which, unless waived by Miragen, requires that Signal have net cash, as defined, of greater than or equal to negative $300,000. If Signal is unable to complete the sale of the MyPRS intellectual property assets and receive the anticipated cash proceeds from that transaction as planned, Signal may have incurred additional expenses that may not allow Signal to meet the closing net cash requirement in the Merger Agreement, and as a consequence, Miragen will have the right to terminate the Merger Agreement.

If Signal is unable to obtain adequate coverage and reimbursement for its tests, it is unlikely that Signal s tests will gain widespread acceptance.

Maintaining and growing revenues from MyPRS depends on the availability of adequate coverage and reimbursement for Signal s tests from third-party payors, including government programs such as Medicare and Medicaid, private insurance plans and managed care programs. Health care providers that order diagnostic services such as MyPRS generally expect that those diagnostic services are covered and reimbursed by third-party payors for all or part of the costs and fees associated with the diagnostic tests they order. If such diagnostic tests are not covered and reimbursed then their patients may be responsible for the entire cost of the test, which can be substantial. Therefore, health care providers generally do not order tests that are not covered and reimbursed by third-party payors in order to avoid subjecting their patients to such financial liability. The existence of adequate coverage and reimbursement for the procedures performed with MyPRS by government and private insurance plans is central to the acceptance of MyPRS and any future services Signal provides. During the past several years, third-party payors have undertaken cost-containment initiatives including different payment methods, monitoring health care expenditures, and anti-fraud initiatives. For example, the Centers for Medicare & Medicaid Services, or CMS, which administers the Medicare program, has taken the position that the algorithm portion of multi-analyte algorithmic assays, or MAAAs, such as MyPRS, is not a clinical laboratory test and is therefore not reimbursable under the Medicare program. Although this position is only applicable to tests with a CMS determined national payment amount, it is possible that the local MACs, who make coverage and payment determinations for tests like MyPRS may adopt this policy and reduce payment for MyPRS. If that were to happen, reimbursement might be made for each gene used in the MyPRS test and

coverage and the amount of reimbursement for the genes Signal uses in MyPRS would be uncertain. Signal may not be able to achieve or maintain profitability if third-party payors deny coverage or reduce their current levels of payment, or if Signal s costs of production increase faster than increases in reimbursement levels. For some

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governmental programs, such as Medicaid, coverage and reimbursement differ from state to state, and some state Medicaid programs may not pay an adequate amount for MyPRS or may make no payment at all. As the portion of the U.S. population over the age of 65 and eligible for Medicare continues to grow, Signal may be more vulnerable to coverage and reimbursement limitations imposed by CMS. Furthermore, the health care industry in the United States has experienced a general trend toward cost containment as government and private insurers seek to control health care costs through various mechanisms, including imposing limitations on payment rates and negotiating reduced contract rates with service providers, among other things. Therefore, Signal cannot be certain that Signal s services will be reimbursed at a level that is sufficient to meet Signal s costs.

There is a scarcity of experienced professionals in the cancer diagnostic industry. If Signal is not able to retain and recruit personnel with the requisite technical skills, Signal may be unable to successfully execute its business strategy.

The specialized nature of Signal s industry results in an inherent scarcity of experienced personnel in the field. Signal s future success depends upon its ability to attract and retain highly skilled personnel (including medical, scientific, technical, commercial, business, regulatory and administrative personnel) necessary to support its anticipated growth, develop Signal s business and perform certain contractual obligations. Given the scarcity of professionals with the scientific knowledge that Signal requires and the competition for qualified personnel among life science businesses, Signal may not succeed in attracting or retaining the personnel it requires to continue and grow Signal s operations. The loss of a key employee, the failure of a key employee to perform in his or her current position or its inability to attract and retain skilled employees could result in Signal s inability to continue to grow Signal s business or to implement its business strategy.

If Signal is unable to increase sales of its laboratory tests and services or to successfully develop and commercialize other indications for its proprietary tests, Signal s revenues will be insufficient for it to achieve profitability.

Signal s revenue is derived primarily from its laboratory testing services. Signal currently offers the MyPRS test through its state-of the-art Clinical Laboratory Improvement Amendments of 1988, or CLIA,-certified, College of American Pathologists, or CAP,-accredited and state licensed laboratory in Little Rock, Arkansas. MyPRS is not assigned a specific Current Procedural Terminology, also referred to as a CPT code, but Signal s local MAC and Blue Cross Blue Shield, or BCBS, of Arkansas have established a specific payment amount for the test, which is billed under a nonspecific code. Signal is in varying stages of research and development for other diagnostic tests that it may offer. Signal does not currently offer any other testing services. If Signal is unable to increase sales of MyPRS or to successfully develop and commercialize other diagnostic tests, Signal will not produce sufficient revenues to become profitable. Signal s laboratory testing services are expensive and may be a negative factor for gaining routine reimbursement.

If pathologists and oncologists decide not to order Signal s diagnostic tests, Signal may be unable to generate sufficient revenue to sustain its business.

To increase awareness and adoption of Signal s molecular diagnostic tests and services, Signal will need to educate oncologists and pathologists on the clinical utility, benefits and value of each type of test Signal provides through published papers, presentations at scientific conferences and one-on-one education sessions by members of its commercial team. In addition, Signal will need to assure oncologists and pathologists of its ability to obtain and maintain adequate reimbursement coverage from third-party payors. Signal may need to hire additional commercial, scientific, technical, selling and marketing and other personnel to support this process. If Signal s educational efforts fail and medical practitioners do not order its diagnostic tests or other tests Signal may develop, utilization of its tests in sufficient volume for Signal to achieve sustained profitability or, perhaps, viability may not be possible.

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Signal s business depends on its ability to successfully develop and commercialize novel cancer diagnostic tests and services, which is time consuming and complex, and Signal s development efforts may fail.

Signal s current business strategy focuses on discovering, developing and commercializing molecular diagnostic tests and services. Signal believes the success of its business depends on its ability to fully commercialize its existing diagnostic tests and services and to develop and commercialize new diagnostic tests. In particular, it is essential to Signal s business strategy that it expand the indications for use of MyPRS. The first additional indications for which Signal hopes MyPRS will be used include MGUS and SMM. Collectively, these precursor conditions are referred to as AMG. However, Signal may be unsuccessful and MyPRS may never be used for these indications. Signal may not succeed because it may never be accepted by the oncologist community, third-party payors may not pay for it, and the recent peer-reviewed publication that could support these indications for MyPRS may not be sufficient to drive adoption support coverage and reimbursement and the results may not be duplicated in additional studies.

In addition, prior to commercializing its diagnostic tests, Signal must undertake time-consuming and costly development activities, sometimes including clinical trials, and may be required to obtain regulatory clearance or approval, which may be denied. This development process involves a high degree of risk, substantial expenditures and will occur over several years. Signal development efforts may fail for many reasons, including:

- failure of the tests at the research or development stage;
- difficulty in accessing archival tissue samples, especially tissue samples with known clinical results; or
- lack of clinical validation data to support the effectiveness of the test.

Tests that appear promising in early development may fail to be validated in subsequent studies, and even if Signal achieves positive results, Signal may ultimately fail to obtain the necessary regulatory clearances, approvals or coverage and reimbursement. There is substantial risk that Signal s research and development projects will not result in commercially viable tests, and that success in early clinical studies will not be replicated in later studies. At any point, Signal may abandon development of a test or be required to expend considerable resources repeating clinical trials, which would adversely impact its ability to generate revenues from that test. In addition, as Signal develops tests, it will have to make significant investments in research, development and marketing resources. If a clinical validation study of a particular test fails to meet its endpoint, Signal might choose to abandon the development of that test. Further, its ability to develop and launch diagnostic tests will likely depend on its receipt of additional funding beyond that obtained through its public offerings. If Signal s discovery and development programs yield fewer commercial tests than Signal expects, it may be unable to execute its business plan, which may adversely affect its business, financial condition and results of operations.

If Signal is unable to execute its marketing strategy for its cancer diagnostic tests and is unable to gain acceptance in the market, Signal may be unable to generate sufficient revenue to sustain its business.

Signal is an early-stage company and has engaged in only limited selling and marketing activities for MyPRS. There is not currently widespread awareness or adoption of its MyPRS testing system. Although Signal believes that MyPRS represents a promising commercial opportunity, it may never gain significant acceptance in the marketplace and therefore may never generate substantial revenue or profits for Signal. This is also true for any additional diagnostic tests Signal may market. Signal will need to establish a market for its diagnostic tests and build that market through

physician education and awareness programs. Gaining acceptance in medical communities requires publication in leading peer-reviewed journals of results from studies using its tests. The process of publication in leading medical journals is subject to a peer review process and peer reviewers may not consider the results of its studies sufficiently novel or worthy of publication. Failure to have its studies published in peer-reviewed journals would limit the adoption of its tests and future coverage and reimbursement decisions for its tests could be negatively affected.

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Signal s ability to successfully market the diagnostic tests that it may develop will depend on numerous factors, including:

- whether health care providers believe its diagnostic tests are clinically useful;
- whether the medical community accepts that its diagnostic tests are sufficiently sensitive and specific to be meaningful in patient care and treatment decisions; and
- whether health insurers, government health programs and other third-party payors will cover and pay for Signal s diagnostic tests and, if so, whether they will adequately reimburse Signal.

If any of these do not occur, Signal could fail to achieve widespread market acceptance of its diagnostic tests and its business would be materially harmed, as would its financial condition and results of operations.

If Signal s tests do not perform as expected, its operating results, reputation and business will suffer.

Signal s success depends on the market s confidence that it can continue to provide reliable, high-quality diagnostic tests. Signal believes that its customers are likely to be particularly sensitive to test defects and errors, such as false positive or false negative results which could affect the patient s eventual diagnosis and/or treatment. As a result, the failure of its tests or services to perform as expected would significantly impair its reputation and the public image of its tests and services, and Signal may be subject to legal claims arising from any defects or errors.

Signal may implement a product recall or voluntary market withdrawal of MyPRS due to test defects or enhancements and modifications, which would significantly increase its costs.

The marketing of MyPRS and any future diagnostic tests that it may develop involves an inherent risk that such tests may prove to be defective. In that event, Signal may voluntarily implement a market withdrawal of such tests or may be required to do so by a regulatory authority. A recall of MyPRS or one of its future diagnostic tests, or a similar product or service offered by another provider, could impair sales of the services Signal markets as a result of confusion concerning the scope of the recall or as a result of the damage to its reputation for quality and safety.

If Signal s sole laboratory facility becomes damaged or inoperable, or Signal is required to vacate the facility, Signal s ability to provide services and pursue its research and development efforts may be jeopardized.

Signal currently derives substantially all of its revenues from its laboratory testing services. Signal does not have any clinical reference laboratory facilities other than its facility in Little Rock, Arkansas. Signal s facilities and equipment could be harmed or rendered inoperable by natural or man-made disasters, including fire, flooding and power outages, which may render it difficult or impossible for Signal to perform its tests or provide laboratory services for some period of time. The inability to perform Signal s tests or the backlog of tests that could develop if its facility is inoperable for even a short period of time may result in the loss of customers or harm to its reputation or relationships with collaborators, and Signal may be unable to regain those customers or repair its reputation in the future. Furthermore, Signal s facilities and the equipment Signal uses to perform its research and development work could be costly and time-consuming to repair or replace, which could further delay its ability to provide testing services.

Additionally, a key component of its research and development process involves using biological samples and the resulting data sets and medical histories, as the basis for its diagnostic test development. In some cases, these samples are difficult to obtain. If the parts of Signal s laboratory facility where it stores these biological samples are damaged or compromised, Signal s ability to pursue its research and development projects, as well as Signal s reputation, could be jeopardized. Signal carries insurance for damage to its property and the disruption of its business, but this insurance may not be sufficient to cover all of Signal s potential losses and may not continue to be available to Signal on acceptable terms, if at all.

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Further, if Signal s laboratory became inoperable, it may not be able to license or transfer its proprietary technology to a third party, with established state licensure and CLIA certification under the scope of which its diagnostic tests could be performed following validation and other required procedures, to perform the tests. Even if Signal finds a third party with such qualifications to perform its tests, such party may not be willing to perform the tests for Signal on commercially reasonable terms. Signal may have to reapply for state licensure and CLIA certification if Signal is unable to find a third party with such qualifications.

If Signal cannot compete successfully with its competitors, Signal may be unable to increase or sustain its revenues or achieve and sustain profitability.

Signal s principal competition comes from the existing mainstream diagnostic methods that pathologists and oncologists use and have used for many years. It may be difficult to change the methods or behavior of the referring pathologists and oncologists to incorporate its molecular diagnostic testing in their practices. However, Signal believes that it can introduce its diagnostic tests successfully due to their clinical utility and the desire of pathologists and oncologists to find solutions for more accurate diagnosis, prognosis and personalized treatment options for MM and AMG patients. But this is not certain and if the health care providers who are in a position to order its tests do not adopt them, it could adversely affect Signal s business.

Signal also faces competition from companies that currently offer or are developing products to profile genes, gene expression or protein biomarkers in various cancers. Personalized genetic diagnostics is a new area of science, and Signal cannot predict what tests others will develop that may compete with or provide results superior to the results Signal is able to achieve with the tests Signal develops. Signal s competitors include public companies such as NeoGenomics, Inc., Quest Diagnostics, Abbott Laboratories, Inc., Johnson & Johnson, Roche Molecular Systems, Inc., Genomic Health, Inc., Myriad Genetics Inc., Qiagen N.V., Foundation Medicine, Inc., Cancer Genetics, Inc., and many private companies, including Agendia B.V. and bioTheranostics, Inc. Another source of competition comes from other scientific teams attempting to develop GEP signatures utilizing other genes or a subset of the genes utilized in Signal s MyPRS test. Two groups of note include the French IFM-15 gene signature and the Netherlands EMC-92 gene signature which have been studied by independent groups and compared to the UAMS GEP test, or MyPRS.

Signal provides services in a segment of the health care industry that is highly fragmented and extremely competitive. Any failure to respond to technological advances and emerging industry standards could impair Signal s ability to attract and retain clients. This industry is characterized by rapid technological change. It is anticipated that competition will continue to increase due to such factors as the potential for commercial applications of biotechnology and the continued availability of investment capital and government funding for cancer-related research. Signal s competitors may succeed in developing diagnostic tests and/or services that are superior to Signal s tests and technologies, including Signal s pipeline tests. This could render its tests obsolete and, as a result, they might not be ordered, thus impairing the viability of Signal s business.

Signal expects that pharmaceutical and biopharmaceutical companies will increasingly focus attention and resources on the personalized diagnostic sector as the potential and prevalence increases for molecularly targeted oncology therapies approved by the FDA along with companion diagnostics. For example, the FDA has approved two such agents Xalkori® (crizotinib) from Pfizer Inc. along with its companion anaplastic lymphoma kinase, fluorescence in situ hybridization (FISH) test from Abbott Laboratories, Inc. and Zelboraf® (vemurafenib) from Genentech USA Incorporated and Daiichi-Sankyo Inc. along with its companion B-RAF kinase V600 mutation test from Roche Molecular Systems, Inc. These two FDA approvals are the second and third instances of simultaneous approvals of a drug and companion diagnostic, the first being the 1998 approval of Genentech, Inc. s Herceptin® (trastuzumab) for HER2 positive breast cancer along with the HercepTest™ from partner Dako A/S.

Signal also face competition from companies such as Genoptix, Inc. (a Novartis AG company), Neogenomics, Inc., Cancer Genetics, Inc., Bio-Reference Laboratories, Inc. (a division of OPKO Health, Inc.), Integrated

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Genetics (a LabCorp Specialty Testing Group) and Foundation Medicine, Inc., which offer products or services or have conducted research to develop genetic profiles, or genetic or protein biomarkers for various cancers. Additionally, projects related to cancer genomics have received increased government funding, both in the United States and internationally. As more information regarding cancer genomics becomes available to the public, Signal anticipates that more products and services aimed at predicting patient outcome as well as identifying targeted treatment options will be developed and that these products and services may compete with the services Signal offers. In addition, competitors may develop their own versions of Signal s tests in countries where Signal did not apply for patents or where Signal s patents have not issued and compete with Signal in those countries, including promoting the use of their test(s) by physicians or patients in other countries.

Many of its present and potential competitors have widespread brand recognition and substantially greater financial and technical resources and development, production and marketing capabilities than Signal does. Others may develop lower-priced, less complex tests that payors, pathologists and oncologists could view as functionally equivalent to Signal s tests, which could force Signal to lower the list price of Signal s tests and impact its operating margins and its ability to achieve profitability. In addition, technological innovations that result in the creation of enhanced diagnostic tools may enable other clinical laboratories, hospitals, physicians or medical providers to provide specialized diagnostic services similar to ours in a more patient-friendly, efficient or cost-effective manner than is currently possible. If Signal cannot compete successfully against current or future competitors, Signal may be unable to increase market acceptance and sales of its tests, which could prevent Signal from increasing or sustaining its revenues or achieving or sustaining profitability.

The loss of Signal s Chairman or key members of its executive management team could adversely affect its business.

Signal s success in implementing its business strategy depends largely on the skills, experience and performance of the Chairman of its board of directors, Bennett S. LeBow, key members of Signal s executive management team and others in key management positions, including Samuel D. Riccitelli, its president and chief executive officer, and Tamara A. Seymour, Signal s chief financial officer. The collective efforts of each of these persons working as a team are critical as Signal continues to develop its technologies, tests and research and development and sales programs. As a result of the difficulty in locating qualified new management, the loss or incapacity of existing members of its executive management team could adversely affect its operations. If Signal were to lose one or more of these key employees, Signal could experience difficulties in finding qualified successors, competing effectively, developing its technologies and implementing its business strategy. Signal s president and chief executive officer, Samuel D. Riccitelli, Signal s chief financial officer, Tamara A. Seymour, and other members of the executive team have employment agreements with Signal. However, the existence of an employment agreement does not guarantee retention of members of its executive management team or its key employees and Signal may not be able to retain those individuals for the duration of or beyond the end of their respective terms.

If Signal were sued for product liability or professional liability, Signal could face substantial liabilities that exceed its resources.

The marketing, sale and use of Signal s tests could lead to the filing of product liability claims were someone to allege that its tests failed to perform as designed. Signal may also be subject to liability for errors in the test results Signal provides to pathologists and oncologists or for a misunderstanding of, or inappropriate reliance upon, the information Signal provides. A product liability or professional liability claim could result in substantial damages and be costly and time-consuming for Signal to defend.

Although Signal believes that its existing product and professional liability insurance is adequate, Signal s insurers may fail to defend Signal or Signal s insurance may not fully protect Signal from the financial impact of defending against product liability or professional liability claims. Any product liability or professional liability claim brought against Signal, with or without merit, could increase its insurance rates or prevent Signal from

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securing insurance coverage in the future. Additionally, any product liability lawsuit could damage its reputation, or cause current clinical partners and collaborators to terminate existing agreements and potential clinical partners to seek other partners, cause customers to terminate their relationship with Signal and potential customers to seek alternative testing solutions, any of which could impact Signal s results of operations.

Declining general economic or business conditions may have a negative impact on Signal s business.

Continuing concerns over U.S. health care reform legislation and energy costs, geopolitical issues, the availability and cost of credit and government stimulus programs in the United States and other countries have contributed to increased volatility and diminished expectations for the global economy. These factors, combined with low business and consumer confidence and high unemployment, precipitated an economic slowdown and recession. If the economic climate does not improve or deteriorates, Signal s business, including its access to patient samples and the addressable market for diagnostic tests that Signal may successfully develop, as well as the financial condition of Signal s suppliers and Signal s third-party payors, could be adversely affected, resulting in a negative impact on Signal s business, financial condition and results of operations.

Signal depends on its information technology and telecommunications systems, and any failure of these systems could harm its business.

Signal depends on information technology and telecommunications systems for significant aspects of its operations. In addition, Signal s third-party billing and collections provider depends upon telecommunications and data systems provided by outside vendors and information Signal provides on a regular basis. These information technology and telecommunications systems support a variety of functions, including test processing, sample tracking, quality control, customer service and support, billing and reimbursement, research and development activities and Signal s general and administrative activities. Information technology and telecommunications systems are vulnerable to damage from a variety of sources, including telecommunications or network failures, malicious human acts and natural disasters. Moreover, despite network security and back-up measures, some of its systems are potentially vulnerable to physical or electronic break-ins, computer viruses and similar disruptive problems. Despite the precautionary measures Signal has taken to prevent unanticipated problems that could affect its information technology and telecommunications systems, failures or significant downtime of Signal s information technology or telecommunications systems or those used by its third-party service providers could prevent Signal from processing tests, providing test results to pathologists, oncologists, billing payors, processing reimbursement appeals, handling patient or physician inquiries, conducting research and development activities and managing the administrative aspects of Signal s business. Any disruption or loss of information technology or telecommunications systems on which critical aspects of its operations depend could have an adverse effect on Signal s business. Furthermore, Signal depends on FedEx as its courier. Any disruption in any of Signal s mail services or transportation logistics could result in spoiled or lost samples, which could reduce revenue. Moreover, Signal is required to comply with laws governing the transmission, security and privacy of health information that require significant compliance costs, and any failure to comply with these laws could result in material criminal and civil penalties and civil liabilities.

Signal or its suppliers and/or manufacturers may be subject to litigation relating to, among other things, payor and customer disputes, regulatory actions, professional liability, intellectual property, employee-related matters, product liability and other potential claims, which could adversely affect its business.

Signal or its suppliers and/or manufacturers may become subject in the ordinary course of business to material litigation related to things, payor or customer disputes, professional liability, regulatory actions, intellectual property, employee-related matters, product liability and other potential claims, as well as investigations by governmental agencies and governmental payors relating to the specialized diagnostic services Signal provides. Responding to these

types of claims, regardless of their merit, could result in significant expense and divert the time, attention and resources of its management. Legal actions could result in substantial monetary damages as well as significant harm to its reputation with Signal s oncologist customers and with payors, which could

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adversely affect Signal s business, financial condition and results of operations. Signal s laboratory directors and other laboratory professionals may be sued, or may be added as an additional party, under physician liability or other liability law for acts or omissions by its lab directors, laboratory personnel, and other employees and consultants, including but not limited to being sued for misdiagnoses or liabilities arising from the professional interpretations of test results. Signal may periodically become involved as defendants in medical malpractice and other lawsuits, and are subject to the attendant risk of substantial damage awards, in particular in connection with Signal s MyPRS test. Signal s laboratory directors are insured for medical malpractice risks on a claims-made basis under traditional professional liability insurance policies. Signal also maintains general liability insurance that covers certain claims to which Signal may be subject. Signal s general insurance does not cover all potential liabilities that may arise, including governmental fines and penalties that it may be required to pay, liabilities it may incur under indemnification agreements and certain other uninsurable losses that Signal may suffer. It is possible that future claims will not be covered by or will exceed the limits of Signal s insurance coverage or that Signal s insurers will refuse to defend Signal against claims. The suppliers and manufacturers of the diagnostic tests it performs, which are critical to the performance of its specialized diagnostic services, may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that their diagnostic tests infringe the intellectual property rights of these third parties. In such event, Signal could no longer have access to, or may be prohibited from marketing or performing, such diagnostic tests unless Signal obtained a license from such third party. A license may not be available on acceptable terms, if at all. If Signal is unable to license diagnostic tests that are important to its specialized diagnostic services, its business, financial condition and results of operations may be adversely affected.

Regulatory Risks Relating to Signal s Business

Signal s commercial success could be compromised if third-party payors, including managed care organizations and Medicare, do not provide coverage and reimbursement, breach, rescind or modify their contracts or reimbursement policies or delay payments for Signal s molecular diagnostic tests.

Pathologists and oncologists may not order Signal s molecular diagnostic tests unless third-party payors, such as managed care organizations and government payors such as Medicare and Medicaid, pay a substantial portion of the test price. Coverage and reimbursement by a third-party payor may depend on a number of factors, including a payor s determination that tests using Signal s technologies are:

- experimental or investigational;
- not medically necessary;
- not appropriate for the specific patient;
- not cost-effective;
- not supported by peer-reviewed publications; and/or

not included in clinical practice guidelines.

Uncertainty surrounds third-party payor reimbursement of any test incorporating new technology, including tests developed using microarrays. Technology assessments of new medical tests and devices conducted by research centers and other entities may be disseminated to interested parties for informational purposes. Third-party payors and health care providers may use such technology assessments as grounds to deny coverage for a test or procedure. To Signal s knowledge, no technology assessments have been performed on its tests to date. However, if any technology assessments on Signal s tests are performed, they could conclude that its tests are not clinically useful and this could result in payor non-coverage decisions, which would adversely affect its business.

Because each payor generally determines for its own enrollees or insured patients whether to cover or otherwise establish a policy to reimburse Signal s diagnostic tests, seeking coverage and reimbursement is a time-consuming and costly process. Signal cannot be certain that coverage for Signal s tests will be provided in the

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future by additional third-party payors or that existing contracts, agreements or policy decisions or reimbursement levels will remain in place or be fulfilled under existing terms and provisions. If Signal cannot obtain coverage and reimbursement from private and governmental payors such as Medicare and Medicaid for Signal s current tests, or new tests or test enhancements that Signal may develop in the future, Signal s ability to generate revenues could be limited, which may have a material adverse effect on Signal s financial condition, results of operations and cash flow. Further, Signal has experienced in the past, and will likely experience in the future, delays and temporary interruptions in the receipt of payments from third-party payors due to missing documentation and other issues, which could cause delay in collecting its revenue.

In some circumstances, being contracted with private third-party payors may limit the amount of reimbursement.

Signal is currently considered a non-contracted provider by a number of private third-party payors because Signal has not entered into a specific contract to provide Signal s specialized diagnostic services to their insured patients at specified rates of reimbursement. If Signal were to become a contracted provider in the future, the amount of overall reimbursement Signal would receive may decrease because Signal could be reimbursed less at a contracted rate than it would be at a non-contracted rate, which could have a negative impact on its revenues. Further, Signal may be unable to collect payments from patients beyond that which is paid by their insurance and may experience lost revenue as a result.

Because of certain Medicare billing rules, Signal may not receive reimbursement for all tests provided to Medicare patients.

Under current Medicare billing rules, claims for Signal s tests performed on Medicare beneficiaries who were hospital patients when the tumor tissue samples were obtained and whose tests were ordered less than 14 days from discharge must be included in the payment that the hospital receives for the patient services provided. Accordingly, Signal must bill individual hospitals for tests performed on Medicare beneficiaries during these timeframes in order to receive payment for its tests. Because Signal generally does not have a written agreement in place with these hospitals that purchase these tests, Signal may not be paid for Signal s tests or may have to pursue payment from the hospital on a case-by-case basis. This could be especially problematic for Signal if the hospital does not receive separate payment from Medicare for its test.

Because a portion of Signal s revenues is from third-party payors with whom Signal is not currently contracted, Signal may be required to make positive or negative adjustments to accounting estimates with respect to contractual allowances, which may adversely affect Signal s results of operations, its credibility with financial analysts and investors, and its stock price.

Signal records revenues net of contractual allowances. Signal estimates contractual allowances for non-contracted insurance companies based on its historical collection experience for each type of payor. In the event that the actual amount of payment received differs from the previously recorded estimate, an adjustment to revenue is made in the current period at the time of final collection and settlement. Signal s estimates of net revenue for non-contracted insurance companies are subject to change based on the contractual status and payment policies of the third-party payors with whom Signal deals. Signal regularly refines its estimates in order to make its estimated revenue as accurate as possible based on Signal s most recent collection experience with each third-party payor. There can be no assurances that Signal will not be required to make similar adjustments to estimates with respect to contractual allowances in the future, which could adversely affect Signal s results of operations, its credibility with financial analysts and investors, and its stock price.

Complying with numerous regulations pertaining to Signal s business is an expensive and time-consuming process, and any failure to comply could result in substantial penalties.

Signal is subject to CLIA, a federal law regulating clinical laboratories that perform testing on specimens derived from humans for the purpose of providing information for the diagnosis, prevention or treatment of disease.

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Signal s clinical laboratory must be certified under CLIA in order for Signal to perform testing on human specimens. In addition, Signal s proprietary tests must also be categorized as part of its CLIA certification so that Signal can offer them in Signal s laboratory. CLIA is intended to ensure the quality and reliability of clinical laboratories in the United States by mandating specific standards in the areas of personnel qualifications, administration, and participation in proficiency testing, patient test management, quality control, quality assurance and inspections. Signal has a current certificate under CLIA to perform high complexity testing. To renew this certificate, Signal is subject to survey and inspection every two years. Moreover, CLIA inspectors may make periodic inspections of its clinical reference laboratory outside of the renewal process. Because Signal is also CAP-accredited, Signal is subject to published accreditation standards to which Signal must conform in order to maintain Signal s accreditation, and subject to periodic unannounced laboratory audits.

The law also requires Signal to maintain a state laboratory license to conduct testing. Signal s laboratory is located in Arkansas and must have an Arkansas state license. Arkansas laws establish standards for day-to-day operation of Signal s clinical reference laboratory, including the training and skills required of personnel and quality control. In addition, several other states require that Signal holds licenses to test specimens from patients in those states. Other states may have similar requirements or may adopt similar requirements in the future. Finally, Signal may be subject to regulation in foreign jurisdictions as Signal seeks to expand international distribution of its tests.

If Signal were to lose its CLIA certificate or Arkansas laboratory license, whether as a result of a revocation, suspension or limitation, Signal would no longer be able to offer its tests, which would limit its revenues and harm Signal s business. If Signal were to lose its license in other states where Signal is required to hold licenses, Signal would not be able to test specimens from those states.

Signal is subject to federal and state health care fraud and abuse laws and regulations and could face substantial penalties if it is unable to fully comply with such laws.

Signal is subject to health care fraud and abuse regulation and enforcement by both the federal government and the states in which Signal conducts its business. These health care laws and regulations include, for example:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from soliciting, receiving, offering or providing remuneration, directly or indirectly, in return for, to induce or to arrange for the referral of an individual for, or the purchase, order or recommendation of, any items or services for which payment may be made under a federal health care program such as the Medicare and Medicaid programs;

- the federal physician self-referral prohibition, commonly known as the Stark Law, which prohibits physicians from referring Medicare or Medicaid patients to providers of designated health services with whom the physician or a member of the physician s immediate family has an ownership interest or compensation arrangement, unless a statutory or regulatory exception applies;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which establishes federal crimes for knowingly and willfully executing a scheme to defraud any health care benefit program or making false statements in connection with the delivery of or payment for health care benefits, items or services;

the federal False Claims Act, which prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;

the federal Physician Payment Sunshine Act requirements under the ACA, which require manufacturers of drugs, devices, biologics and medical supplies to report to HHS information related to payments and other transfers of value made to or at the request of covered recipients, such as physicians and teaching hospitals, and physician ownership and investment interests in such manufacturers. Payments made to physicians and research institutions for clinical trials are included within the ambit of this law; and

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state law equivalents of each of the above federal laws, which may apply more broadly, contain additional restrictions, or carry different types of penalties.

Signal seeks to comply with these laws. However, it is possible that Signal could be the subject of a government investigation regarding its compliance with these or other laws and that the government could take the position that Signal is not in compliance with one or more of them. In such case, Signal may be judged to be in violation of those laws and subject to civil and criminal penalties. In addition, many of these laws and regulations are vague or indefinite and have not been interpreted by the courts or regulatory agencies. These laws and regulations may be interpreted or applied by a prosecutorial, regulatory or judicial authority in a manner that could subject Signal to liability and/or require Signal to make changes in Signal s operations.

Signal believes that federal and state governments continue to strengthen their enforcement efforts against health care fraud. In addition, the ACA increases the funding, power, penalties and remedies to pursue suspected cases of fraud and abuse and provides the government with expanded opportunities to pursue actions under the federal Anti-Kickback Statute, the False Claims Act, and the Stark Law. For example, the ACA narrowed the public disclosure bar under the False Claims Act, allowing increased opportunities for whistleblower litigation. In addition, the legislation modified the intent standard under the federal Anti-Kickback Statute, making it easier for prosecutors to prove that alleged violators had met the requisite knowledge requirement. The ACA and final regulations promulgated thereunder also require Medicare Part A and B providers and suppliers to report and return Medicare overpayments by the later of 60 days after the date on which the overpayment was identified or, if applicable, the date any corresponding cost report is due. Overpayments are considered to be identified when the provider or supplier has or should have, through the exercise of reasonable diligence, determined that it has received an overpayment, and quantified the amount of the overpayment. The ACA also provides that claims that include items or services resulting from a violation of the Anti-Kickback Statute constitutes a false or fraudulent claims for purposes of the False Claims Act. Any action brought against Signal for violation of these laws or regulations, even if Signal successfully defends against it, could cause Signal to incur significant legal expenses and divert Signal s management s attention from the operation of its business. If Signal s operations are found to be in violation of any of these laws and regulations, Signal may be subject to any applicable penalty associated with the violation, including civil and criminal penalties, damages and fines, and/or exclusion from participation in Medicare, Medicaid or other state or federal health care programs, Signal could be required to refund payments received by Signal, and Signal could be required to curtail or cease its operations. Any of the foregoing consequences could seriously harm its business, its financial condition and results of operations.

Signal is required to comply with laws governing the transmission, security and privacy of health information that require significant compliance costs, and any failure to comply with these laws could result in material criminal and civil penalties.

Under the administrative simplification provisions of HIPAA, HHS has issued regulations which establish uniform standards governing the conduct of certain electronic health care transactions and protecting the privacy and security of Protected Health Information, or PHI, used or disclosed by health care providers and other covered entities. Three principal regulations with which Signal is currently required to comply have been issued in final form under HIPAA: privacy regulations, security regulations and standards for electronic transactions.

The privacy regulations cover the use and disclosure of PHI by health care providers. It also sets forth certain rights that an individual has with respect to his or her PHI maintained by a health care provider, including the right to access or amend certain records containing PHI or to request restrictions on the use or disclosure of PHI. Signal has also implemented policies, procedures and standards to comply appropriately with the final HIPAA security regulations, which establish requirements for safeguarding the confidentiality, integrity and availability of PHI, which is electronically transmitted or electronically stored. The HIPAA privacy and security regulations establish a uniform

federal floor and do not supersede state laws that are more stringent or provide individuals with greater rights with respect to the privacy or security of, and access to, their records containing PHI. As a result, Signal is required to comply with both HIPAA privacy regulations and varying state privacy and security

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laws. Almost all U.S. states now require notification to affected individuals and state authorities, as well as the media in certain cases, in the event of a breach of the security of personal information (including PHI in a few states), often with significant financial penalties for noncompliance.

The Health Information Technology for Economic and Clinical Health Act, or HITECH Act, enacted pursuant to the American Recovery and Reinvestment Act of 2009, or ARRA, made sweeping changes to the health information privacy and security regulations of HIPAA by expanding the scope and application of the statute. These changes include, among other things: (1) establishing an affirmative obligation to provide patient data breach notification in the event of the unauthorized acquisition, access, use or disclosure of unsecured PHI; (2) elaborating upon the standard for minimum necessary uses and disclosures of PHI by a covered entity; (3) restricting certain uses of PHI for marketing purposes (by expanding the definition of marketing activities requiring authorization); (4) prohibiting certain sales of PHI; (5) establishing an affirmative obligation to provide an accounting of disclosures made for payment, treatment and health care operations (up to three years made through an electronic health record); (6) requiring covered entities to agree to individuals requests to restrict disclosure of PHI in certain circumstances; (7) applying the security regulations and certain provisions of the privacy regulations to business associates; and (8) modifying an individuals right to access PHI in an electronic format. HHS issued modifications to the HIPAA Regulations, effective March 26, 2013, implementing some of these changes including the obligation to provide patient data breach notifications, which subject the company to additional administrative requirements in the United States. With regard to the accounting of disclosures, the HITECH Act provides for removing the exception in the existing HIPAA privacy regulations accounting of disclosures of PHI requirement for disclosures of PHI for payment, treatment, and health care operations purposes made through an electronic health record (within the past three years). HHS issued proposed regulations to implement this provision of the HITECH Act in May 2011, but those regulations have not been finalized.

The HITECH Act also implemented measures to strengthen enforcement of HIPAA and increased applicable penalties for HIPAA violations. Penalties are now tiered and range from $100 to $50,000 per violation with an annual cap for the same violations of $25,000 to $1,500,000. The Office for Civil Rights of the HHS, or the OCR, has increased enforcement activities and has recently levied large penalties for violations. In addition, as mandated by the HITECH Act, OCR has begun an audit program to assess compliance by covered entities and their business associates with the HIPAA privacy and security rules and breach notification standards.

Signal seeks to comply with HIPAA privacy regulations and state privacy laws. In addition, Signal is in the process of taking necessary steps to comply with HIPAA s standards for electronic transactions, which establish standards for common health care transactions. Given the complexity of HIPAA, the HITECH Act and state privacy restrictions, the possibility that the regulations may change, and the fact that the regulations are subject to changing and potentially conflicting interpretation, Signal s ability to comply with HIPAA, the HITECH Act and state privacy requirements is uncertain and the costs of compliance are significant. To the extent that Signal or its third-party billing company submit electronic health care claims and payment transactions that do not comply with the electronic data transmission standards established under HIPAA and the HITECH Act, payments to Signal may be delayed or denied. Additionally, the costs of complying with any changes to HIPAA, the HITECH Act and state privacy restrictions may have a negative impact on Signal s operations. Signal could be subject to criminal penalties and civil sanctions for failing to comply with HIPAA, the HITECH Act and state privacy restrictions, which could result in the incurrence of significant monetary penalties.

Risks Related to Signal s Reliance on Third Parties

Signal licenses its billing and collections web-based software platform from a third-party provider. Signal s provider may fail in its obligations to maintain the system and thereby reduce its cash collections and harm its

business.

Billing for laboratory tests is complicated and is subject to extensive and non-uniform rules and administrative requirements. Missing or incorrect information on requisitions adds complexity to and slows the billing process,

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creates backlogs and increases the aging of accounts receivable and bad debt expenses. Failure to timely or correctly bill may lead to Signal not being reimbursed for its services or an increase in aging of Signal s accounts receivable. In addition, failure to comply with applicable federal and state laws relating to billing, including, but not limited, to the federal False Claims Act may lead to various penalties including civil and criminal fines and penalties, recoupment efforts, and exclusion from participation in Medicare and other federal health care programs. Signal relies heavily on a single third party to provide Signal with key software for Signal s billing. If that third party is unable or unwilling to provide these software systems to Signal for any reason, or violates the law, Signal may not be able to submit claims promptly or at all and Signal may be subject to an investigation and potential civil and criminal penalties. Delays in invoicing can lead to delays in collections, and inaccuracies in its billing could result in lost revenue. If Signal fails to adapt quickly and effectively to changes affecting Signal s costs, pricing and billing, its profitability and cash flow will be adversely affected.

Signal depends on third parties for the supply of certain tissue samples and biological materials that Signal uses in its research and development efforts. If these costs increase or Signal s third-party collaborators terminate their relationship with Signal, Signal s business may be materially harmed.

Under standard clinical practice in the United States, tumor biopsies removed from patients are chemically preserved, embedded in paraffin wax and stored. Signal s clinical development relies on its ability to access these archived tumor biopsy samples, as well as information pertaining to their associated clinical outcomes. Other companies often compete with Signal for access. Additionally, the process of negotiating access to archived samples is lengthy, because it typically involves numerous parties and approvals to resolve complex issues such as usage rights, institutional review board approval, privacy rights, publication rights, intellectual property ownership and research parameters.

UAMS and other institutions provide Signal with tissue samples and other biological materials that Signal uses in developing and validating its tests. Signal does not have written agreements with some of these third parties, and, in many of the cases in which the agreements are in writing, Signal s relationships with such third parties are terminable on 30 days notice or less. Disagreements or disputes might cause delays or termination of the research, development or commercialization of testing systems or additional test indications, might lead to additional responsibilities or costs to Signal or might result in litigation or arbitration, any of which could divert management attention and resources and be time-consuming and expensive. If one or more of these suppliers terminate their relationship with Signal, Signal will need to identify other third parties to provide Signal with tissue samples and biological materials, which could result in a delay in its research and development activities and negatively affect its business. In addition, as Signal grows, research and academic institutions may begin to seek financial contributions from Signal, which may negatively affect Signal s results of operations. Potential suppliers may elect not to work with Signal based on their assessment of Signal s financial, regulatory or intellectual property position. Even if it establishes new agreements, this may not result in the successful development of future testing systems or additional test indications.

Signal relies on a limited number of third parties for manufacture and supply of all of its laboratory instruments, tests and materials, and Signal may not be able to find replacement suppliers or manufacturers in a timely manner in the event of any disruption, which could adversely affect its business.

Signal relies on third parties for the manufacture and supply of all of Signal s laboratory instruments, equipment and materials, such as reagents, microarray chips and disposable test kits, that Signal needs to perform its specialized diagnostic services, and rely on a limited number of suppliers for certain laboratory materials and some of the laboratory equipment with which Signal performs its diagnostic services. Signal does not have long-term contracts with its suppliers and manufacturers that commit them to supply equipment and materials to Signal. Certain of its suppliers provide Signal with analyte specific regents, or ASRs, which serve as building blocks in the diagnostic tests

Signal conducts in its laboratory. These suppliers are subject to regulation by the FDA, and must comply with federal regulations related to the manufacture and distribution of ASR products. Because Signal cannot ensure the actual production or manufacture of such critical equipment and materials, or

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the ability of its suppliers to comply with applicable legal and regulatory requirements, Signal may be subject to significant delays caused by interruption in production or manufacturing. If any of its third-party suppliers or manufacturers were to become unwilling or unable to provide this equipment or these materials in required quantities or on Signal s required timelines, Signal would need to identify and acquire acceptable replacement sources on a timely basis. While Signal has developed alternate sourcing strategies for the equipment and materials it uses, Signal cannot be certain that these strategies will be effective and even if Signal were to identify other suppliers and manufacturers for the equipment and materials Signal needs to perform its specialized diagnostic services, there can be no assurance that Signal will be able to enter into agreements with such suppliers and manufacturers or otherwise obtain such items on a timely basis or on acceptable terms, if at all. If Signal encounters delays or difficulties in securing necessary laboratory equipment or materials, including consumables, Signal will face an interruption in its ability to perform its specialized diagnostic services and experience other disruptions that would adversely affect its business, results of operations and financial condition.

Intellectual Property Risks Related to Signal s Business

If Signal is unable to maintain intellectual property protection, its competitive position could be harmed.

Signal s ability to protect its proprietary discoveries and technologies affects its ability to compete and to achieve sustained profitability. Currently, Signal relies on a combination of issued U.S. patents, U.S. and foreign patent applications, copyrights, trademarks and trademark applications, confidentiality or non-disclosure agreements, material transfer agreements, licenses, work-for-hire agreements and invention assignment agreements to protect Signal s intellectual property rights. Signal also maintains certain company know-how, trade secrets and technological innovations designed to provide Signal with a competitive advantage in the market place as trade secrets.

Currently, Signal is the worldwide exclusive licensee, in Signal s licensed field, and the owner of 14 issued patents (12 issued U.S. patents, one issued European patent validated in nine countries: Switzerland, Germany, Denmark, Spain, France, United Kingdom, Italy, Netherlands, and Sweden, and one issued Japanese patent) and 11 pending patent applications, which include both U.S. and foreign patent applications, relating to various aspects of its technology. Of the 11 pending patent applications, two are owned outright by Signal Genetics, Inc. Signal s exclusive field of use covers, inter alia, therapeutic, diagnostic, prognostic, and personalized medicine applications worldwide, excluding applications using FISH and some claims directly covering DKK1 inhibitors and their uses.

While Signal intends to pursue additional patent applications, it is possible that Signal s pending patent applications and any future applications may not result in issued patents. Even if patents are issued, third parties may independently develop similar or competing technology that avoids the claims of Signal s patents or may challenge the validity of its patents. Further, Signal cannot be certain that the steps it has taken will prevent the misappropriation of Signal s trade secrets and other confidential information as well as the misuse of its patents and other intellectual property, particularly in foreign countries where Signal has not filed for patent protection.

From time to time the U.S. Supreme Court, other federal courts, the U.S. Congress or the U.S. Patent and Trademark Office, or USPTO, as well as counterpart agencies and bodies in corresponding foreign jurisdictions, may change the standards of patentability and any such changes could have a negative impact on its business.

For instance, on October 30, 2008, the Court of Appeals for the Federal Circuit issued a decision that methods or processes cannot be patented unless they are tied to a machine or involve a physical transformation. The U.S. Supreme Court later reversed that decision in Bilski v. Kappos, or Bilski, finding that the machine-or-transformation test is not the only test for determining patent eligibility. The Court, however, declined to specify how and when processes are patentable. On March 20, 2012, in Mayo v. Prometheus, or Mayo, the U.S. Supreme Court reversed the Federal

Circuit s application of Bilski and invalidated a patent focused on a diagnostic process

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because the patent claim embodied a law of nature. On July 30, 2012, the USPTO released a memorandum titled *2012 Interim Procedure for Subject Matter Eligibility Analysis of Process Claims Involving Laws of Nature,* with guidelines for determining patentability of diagnostic or other processes in line with the Mayo decision. On June 13, 2013, in Association for Molecular Pathology v. Myriad Genetics, or Myriad, the Supreme Court held that a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated, but cDNA is patent eligible because it is not naturally occurring. The Supreme Court s decision reversed in part and affirmed in part the earlier decision of the Federal Circuit that both isolated genes and cDNA were patent eligible, however, the Supreme Court specifically did not address the patentability of any method claims involving the use of such isolated genes. On March 4, 2014, the USPTO released a memorandum titled *2014 Procedure For Subject Matter Eligibility Analysis Of Claims Reciting Or Involving Laws Of Nature/Natural Principles, Natural Phenomena, And/Or Natural Products*, which Signal refers to as the March 4, 2014 memorandum. This memorandum provides guidelines for the USPTO s new examination procedure for subject matter eligibility under 35 U.S.C. §101 for claims embracing natural products or natural principles. On December 16, 2014, the USPTO issued a *2014 Interim Guidance on Patent Subject Matter Eligibility*, which Signal refers to as the 2014 Interim Guidance, for use by USPTO personnel in determining subject matter eligibility in view of recent decisions by the U.S. Supreme Court, which superseded the March 4, 2014 memorandum. On July 2015, the USPTO published an updated guidance document titled *July 2015 Update on Subject Matter Eligibility* that includes new examples and discussion of relevant issues. Although the guidelines do not have the force of law, patent examiners have been instructed to follow them.

Some aspects of Signal s technology involve products and/or processes that may be subject to this evolving standard and Signal cannot guarantee that any of its pending claims will be patentable as a result of such evolving standards or that issued patents will be held valid, if challenged under these changing standards.

In addition, on February 5, 2010, the Secretary s Advisory Committee on Genetics, Health and Society voted to approve a report titled *Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests*. That report defines patent claims on genes broadly to include claims to isolated nucleic acid molecules as well as methods of detecting particular sequences or mutations. The report also contains six recommendations, including the creation of an exemption from liability for infringement of patent claims on genes for anyone making, using, ordering, offering for sale or selling a test developed under the patent for patient care purposes, or for anyone using the patent-protected genes in the pursuit of research. The report also recommended that the Secretary should explore, identify and implement mechanisms that will encourage more voluntary adherence to current guidelines that promote nonexclusive in-licensing of diagnostic genetic and genomic technologies. It is unclear whether the HHS will act upon these recommendations, or if the recommendations would result in a change in law or process that could negatively impact its patent portfolio or future research and development efforts.

Signal may face intellectual property infringement claims that could be time-consuming and costly to defend, and could result in Signal s loss of significant rights and the assessment of treble damages.

From time to time Signal may face intellectual property infringement, misappropriation, or invalidity/non-infringement claims from third parties. Some of these claims may lead to litigation. The outcome of any such litigation can never be guaranteed, and an adverse outcome could affect Signal negatively. For example, were a third party to succeed on an infringement claim against Signal, Signal may be required to pay substantial damages (including up to treble damages if such infringement were found to be willful). In addition, Signal could face an injunction, barring Signal from conducting the allegedly infringing activity. The outcome of the litigation could require Signal to enter into a license agreement which may not be under acceptable, commercially reasonable, or practical terms or Signal may be precluded from obtaining a license at all.

It is also possible that an adverse finding of infringement against Signal may require Signal to dedicate substantial resources and time in developing non-infringing alternatives, which may or may not be possible. In the case of diagnostic tests, Signal would also need to include non-infringing technologies which would require

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Signal to re-validate its tests. Any such re-validation, in addition to being costly and time consuming, may be unsuccessful.

Finally, Signal may initiate claims to assert or defend its own intellectual property against third parties. If one or more of its patents were held to be invalid or not infringed, Signal might not be able to exclude others from offering similar or identical tests to ours. Any intellectual property litigation, irrespective of whether Signal is the plaintiff or the defendant, and regardless of the outcome, is expensive and time-consuming, and could divert its management s attention from its business and negatively affect its operating results or financial condition.

Risks Related to Ownership of Signal s Common Stock

The price of Signal s common stock may be volatile and fluctuate substantially, which could result in substantial losses for Signal stockholders.

Signal s stock price is likely to be volatile. The stock market in general and the market for smaller diagnostic services companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, Signal stockholders may not be able to sell its common stock at or above the price they paid for it. The market price for Signal s common stock may be influenced by many factors, including:

- announcements related to the Merger;
- issuances of new equity securities pursuant to a future offering, including issuances of preferred stock;
- the success of competitive products, services or technologies;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in Signal s financial results or those of companies that are perceived to be similar to Signal;
- changes in the structure of health care payment systems;

market conditions in the diagnostic services sector;

general economic, industry and market conditions; and

the other factors described in this Risk Factors section.

Provisions in Signal s corporate charter documents and under Delaware law could make an acquisition of Signal, which may be beneficial to its stockholders, more difficult and may prevent attempts by its stockholders to replace or remove its current management.

Provisions in Signal s corporate charter and its bylaws may discourage, delay or prevent a merger, acquisition or other change in control of Signal s company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of Signal s common stock, thereby depressing the market price of Signal s common stock. In addition, because Signal s board of directors is responsible for appointing the members of its management team, these provisions may frustrate or prevent any attempts by Signal stockholders to replace or remove its current management by making it more difficult for stockholders to replace members of Signal s board of directors. Among other things, these provisions state that:

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

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Signal s bylaws may be amended or repealed by its board of directors or Signal stockholders;

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

Signal s board of directors will be authorized to issue, without stockholder approval, preferred stock, the rights of which will be determined at the discretion of the 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 Signal s board of directors does not approve;

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

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

Moreover, because Signal is incorporated in Delaware, Signal is governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of Signal s outstanding voting stock from merging or combining with Signal for a period of three years after the date of the transaction in which the person acquired in excess of 15% of Signal s outstanding voting stock, unless the Merger or combination is approved in a prescribed manner.

Signal s failure to meet the continued listing requirements of The NASDAQ Capital Market could result in a delisting of its common stock.

The listing standards of NASDAQ provide, among other things, that a company may be delisted if the bid price of its stock drops below $1.00 for a period of 30 consecutive business days. The bid price of Signal s stock has recently been below $1.00 for a period of greater than 30 consecutive business days. As such, on November 24, 2015, Signal received a notice from The NASDAQ Listing Qualifications Department informing Signal that it must regain compliance with listing requirements or face delisting. After an initial 180-day grace period, Signal received a second letter from NASDAQ dated May 25, 2016 regarding the expiration of the 180-day grace period and granting Signal a second 180-day grace period until November 21, 2016. In order to regain compliance, the bid price of Signals common stock must close at a price of at least $1.00 per share for a minimum of 10 consecutive business days prior to November 21, 2016. The notice stated that NASDAQ will provide Signal with written notification when its common stock has regained compliance. In order to achieve compliance this listing standard, Signal implemented a one-for-15 reverse split of its common stock effective as of 5:01 p.m. Eastern Time on November 4, 2016. On November 22, 2016, NASDAQ notified Signal that it had regained compliance with the minimum bid price requirement for its common stock. While this reverse split of Signal common stock allowed Signal to regain compliance with the listing standards of The NASDAQ Capital Market, there is no guarantee that Signal will be able to maintain compliance with these requirements or that its common stock will not again fall below the minimum bid price requirements for The NASDAQ Capital Market.

While Signal is exercising diligent efforts to maintain the listing of its common stock on NASDAQ, it is possible that Signal may fail to satisfy one of the other the continued listing requirements of The NASDAQ Capital Market, such as the corporate governance requirements or the minimum shareholders equity, publicly held shares or market value of publicly held shares requirements. If that were to occur, NASDAQ may take steps to delist Signal s common stock.

Such a delisting would likely have a negative effect on the price of Signal s common stock and would impair your ability to sell or purchase Signal s common stock when you wish to do so. In the event of a delisting, Signal would take actions to restore Signal s compliance with NASDAQ s listing requirements, but Signal can provide no assurance that any such action taken by Signal would allow its common stock to become listed again, stabilize the market price or improve the liquidity of its common stock, prevent Signal s common stock from dropping below the NASDAQ minimum bid price requirement again or prevent future non-compliance with NASDAQ s listing requirements. Further, if Signal were to be delisted from The NASDAQ Capital Market, its common stock would cease to be recognized as covered securities and Signal would be subject to regulation in each state in which Signal offers its securities.

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Delisting from NASDAQ could adversely affect Signal s ability to raise additional financing through the public or private sale of equity securities, would significantly affect the ability of investors to trade its securities and would negatively affect the value and liquidity of Signal s common stock. Delisting could also have other negative results, including the potential loss of confidence by employees, the loss of institutional investor interest and fewer business development opportunities.

If Signal s shares become subject to the penny stock rules, it may be more difficult to sell Signal shares.

The SEC has adopted rules that regulate broker-dealer practices in connection with transactions in penny stocks. Penny stocks are generally equity securities with a price of less than $5.00 (other than securities registered on certain national securities exchanges or authorized for quotation on certain automated quotation systems, provided that current price and volume information with respect to transactions in such securities is provided by the exchange or system). The OTC Bulletin Board does not meet such requirements and if the price of Signal s common stock remains less than $5.00 and Signal is no longer listed on a national securities exchange, its common stock may be deemed a penny stock. The penny stock rules require a broker-dealer, prior to a transaction in a penny stock not otherwise exempt from those rules, to deliver a standardized risk disclosure document containing specified information. In addition, the penny stock rules require that prior to effecting any transaction in a penny stock not otherwise exempt from those rules, a broker-dealer must make a special written determination that the penny stock is a suitable investment for the purchaser and receive: (i) the purchaser s written acknowledgment of the receipt of a risk disclosure statement; (ii) a written agreement to transactions involving penny stocks; and (iii) a signed and dated copy of a written suitability statement. These disclosure requirements may have the effect of reducing the trading activity in the secondary market for Signal s common stock, and therefore stockholders may have difficulty selling their shares.

An active trading market for Signal s common stock may not develop.

Prior to Signal s initial public offering in June 2014, there was no public market for its common stock. The listing of Signal s common stock on The NASDAQ Capital Market does not assure that a meaningful, consistent and liquid trading market exists. Although Signal s common stock is listed on The NASDAQ Capital Market, trading volume in its common stock has been limited and an active trading market for Signal s shares may never develop or be sustained. If an active market for Signal s common stock does not develop, it may be difficult for investors to sell their shares without depressing the market price for the shares or at all.

Reports published by securities or industry analysts, including projections in those reports that exceed Signal s actual results, could adversely affect its common stock price and trading volume.

Securities research analysts may establish and publish their own periodic projections for Signal s business. These projections may vary widely from one another and may not accurately predict the results Signal actually achieves. Signal s stock price may decline if its actual results do not match securities research analysts projections. Similarly, if one or more of the analysts who writes reports on Signal downgrades its stock or publishes inaccurate or unfavorable research about its business, Signal s stock price could decline. If one or more of these analysts ceases coverage of Signal s company or fails to publish reports on Signal regularly, Signal s stock price or trading volume could decline. While Signal expects securities research analyst coverage, if no securities or industry analysts begin to cover Signal, the trading price for its stock and the trading volume could be adversely affected.

Future sales of Signal s common stock, or the perception that future sales may occur, may cause the market price of its common stock to decline, even if its business is doing well.

Sales of substantial amounts of Signal s common stock in the public market, or the perception that these sales may occur, could materially and adversely affect the price of its common stock and could impair its ability to

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raise capital through the sale of additional equity securities. Signal maintains a shelf registration statement on Form S-3 with the SEC pursuant to which Signal may, from time to time, sell up to an aggregate of $50 million of its common stock, preferred stock, debt securities, warrants, rights and units. Signal has established an at-the-market offering pursuant to which Signal may offer and sell shares of its common stock, if and when Signal s public float increases. Sales of securities under the registration statement will result in dilution of its stockholders and could cause its stock price to fall.

Signal is an emerging growth company, and the reduced disclosure requirements applicable to emerging growth companies may make its common stock less attractive to investors.

Signal is an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company for up to five years. For so long as Signal remains an emerging growth company, Signal is permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced *Management s Discussion and Analysis of Financial Condition and Results of Operations* disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of its internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor s report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a non-binding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

Signal has taken advantage of reduced reporting burdens in its periodic disclosure reports. In particular, Signal has not included all of the executive compensation related information that would be required if Signal were not an emerging growth company. Signal cannot predict whether investors will find Signal s common stock less attractive if Signal relies on these exemptions. If some investors find Signal s common stock less attractive as a result, there may be a less active trading market for its common stock and its stock price may be more volatile.

Signal has elected to avail itself of the extended transition period for adopting new or revised accounting standards available to emerging growth companies under the JOBS Act and will, therefore, not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies, which could make Signal s common stock less attractive to investors.

The JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. Signal has elected to avail itself of this extended transition period for adopting new or revised accounting standards and therefore, Signal will not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. As a result of this election, its financial statements may not be comparable to companies that comply with public company effective dates.

Signal cannot predict whether investors will find its stock less attractive as a result of this election. If some investors find Signal s common stock less attractive as a result of this election, there may be a less active trading market for Signal s common stock and its stock price may be more volatile.

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Since Signal s initial public offering in June 2014, Signal has incurred significantly increased costs and its management has had to devote substantial time as a result of operating as a public company; and such costs are expected to further increase after Signal is no longer an emerging growth company.

As a public company, Signal incurs significant legal, accounting and other expenses that Signal did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The NASDAQ Capital Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Signal s management and other personnel have had to devote a substantial amount of time to these compliance initiatives since becoming a public company. Moreover, these rules and regulations have increased its legal and financial compliance costs and have made certain activities more time-consuming and costly.

Because Signal only recently became a public company, Signal cannot yet predict or estimate the costs Signal may incur in the future with respect to these compliance initiatives or the timing of such costs. In addition, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, as an emerging growth company, Signal is not required to include an attestation report on internal control over financial reporting issued by its independent registered public accounting firm in its annual report. To achieve compliance with Section 404 within the prescribed period, Signal will be engaged in a process to document and evaluate its internal control over financial reporting, which is both costly and challenging. In this regard, Signal will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite Signal s efforts, there is a risk that Signal will not be able to conclude, within the prescribed timeframe or at all, that its internal control over financial reporting is effective as required by Section 404. If Signal identifies one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of its financial statements.

Because Signal does not anticipate paying any cash dividends on its capital stock in the foreseeable future, capital appreciation, if any, will be Signal s sole source of gain.

Signal does not anticipate paying future dividends on its capital stock. Signal currently intends to retain all of its future earnings, as applicable, to finance the growth and development of its business. In addition, the terms of any future debt agreements may preclude Signal from paying dividends. As a result, capital appreciation, if any, of Signal s common stock will be your sole source of gain for the foreseeable future.

Certain of Signal s net operating loss carryforwards have been limited.

Net operating losses incurred by Signal as of June 17, 2014 and prior to the corporate conversion of Signal Genetics LLC into Signal Genetics, Inc. have been used by the members of Signal Genetics LLC to offset gains on other interests and are therefore not able to be carried forward to Signal. The net operating loss carryforward for federal tax purposes held by Signal after the corporate conversion through December 31, 2015 totaled $10.6 million.

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Risks Related to Miragen s Financial Condition and Capital Requirements

Miragen has incurred losses since its inception, has a limited operating history on which to assess its business, and anticipates that it will continue to incur significant losses for the foreseeable future.

Miragen is a clinical development-stage biopharmaceutical company with a limited operating history. Miragen has incurred net losses in each year since its inception in 2006, including net losses of $15.7 million and $5.9 million for the years ended December 31, 2015 and 2014, respectively, and $11.3 million for the nine months ended September 30, 2016. As of September 30, 2016, Miragen had an accumulated deficit of $61.1 million.

As of September 30, 2016, Miragen had cash and cash equivalents of $24.6 million. In September 2016, Miragen received $16.1 million in financing through a follow-on sale of its Series C preferred stock. Additionally, in October 2016, Miragen entered into the Subscription Agreement pursuant to which specified investors agreed to purchase, immediately prior to the consummation of the Merger, shares of Miragen common stock for an aggregate purchase price of $40.7 million. Miragen will continue to require substantial additional capital to continue its clinical development and potential commercialization activities. Accordingly, Miragen will need to raise substantial additional capital to continue to fund its operations. The amount and timing of its future funding requirements will depend on many factors, including the pace and results of its clinical development efforts. Failure to raise capital as and when needed, on favorable terms or at all, would have a negative impact on its financial condition and its ability to develop its product candidates.

Miragen has devoted substantially all of its financial resources to identify, acquire, and develop its product candidates, including conducting clinical trials and providing general and administrative support for its operations. To date, Miragen has financed its operations primarily through the sale of equity securities and convertible promissory notes. The amount of its future net losses will depend, in part, on the rate of its future expenditures and its ability to obtain funding through equity or debt financings, strategic collaborations, or grants. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. Miragen expects losses to increase as it completes Phase 1 development and advances into Phase 2 development its lead product candidates. Miragen has not yet commenced pivotal clinical trials for any product candidate and it may be several years, if ever, before Miragen completes pivotal clinical trials and has a product candidate approved for commercialization. Miragen expects to invest significant funds into the research and development of its current product candidates to determine the potential to advance these product candidates to regulatory approval.

If Miragen obtains regulatory approval to market a product candidate, its future revenue will depend upon the size of any markets in which its product candidates may receive approval, and its ability to achieve sufficient market acceptance, pricing, reimbursement from third-party payors, and adequate market share for its product candidates in those markets. Even if Miragen obtains adequate market share for its product candidates, because the potential markets in which its product candidates may ultimately receive regulatory approval could be very small, Miragen may never become profitable despite obtaining such market share and acceptance of its products.

Miragen expects to continue to incur significant expenses and increasing operating losses for the foreseeable future and its expenses will increase substantially if and as Miragen:

- continues the clinical development of its product candidates;

continues efforts to discover new product candidates;

undertakes the manufacturing of its product candidates or increases volumes manufactured by third parties;

advances its programs into larger, more expensive clinical trials;

initiates additional pre-clinical, clinical, or other trials or studies for its product candidates;

seeks regulatory and marketing approvals and reimbursement for its product candidates;

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establishes a sales, marketing, and distribution infrastructure to commercialize any products for which Miragen may obtain marketing approval and market for itself;

seeks to identify, assess, acquire, and/or develop other product candidates;

makes milestone, royalty or other payments under third-party license agreements;

seeks to maintain, protect, and expand its intellectual property portfolio;

seeks to attract and retain skilled personnel; and

experiences any delays or encounters issues with the development and potential for regulatory approval of its clinical candidates such as safety issues, clinical trial accrual delays, longer follow-up for planned studies, additional major studies, or supportive studies necessary to support marketing approval.

Further, the net losses Miragen incurs may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of its results of operations may not be a good indication of its future performance.

Miragen has never generated any revenue from product sales and may never be profitable.

Miragen has no products approved for commercialization and has never generated any revenue. Miragen s ability to generate revenue and achieve profitability depends on its ability, alone or with strategic collaborators, to successfully complete the development of, and obtain the regulatory and marketing approvals necessary to commercialize one or more of its product candidates. Miragen does not anticipate generating revenue from product sales for the foreseeable future. Miragen s ability to generate future revenue from product sales depends heavily on its success in many areas, including but not limited to:

completing research and development of its product candidates;

obtaining regulatory and marketing approvals for its product candidates;

manufacturing product candidates and establishing and maintaining supply and manufacturing relationships with third parties that are commercially feasible, meet regulatory requirements and Miragen s supply needs in sufficient quantities to meet market demand for its product candidates, if approved;

marketing, launching and commercializing product candidates for which Miragen obtains regulatory and marketing approval, either directly or with a collaborator or distributor;

gaining market acceptance of its product candidates as treatment options;

addressing any competing products;

protecting and enforcing its intellectual property rights, including patents, trade secrets, and know-how;

negotiating favorable terms in any collaboration, licensing, or other arrangements into which Miragen may enter;

obtaining reimbursement or pricing for its product candidates that supports profitability; and

attracting, hiring, and retaining qualified personnel.

Even if one or more of the product candidates that Miragen develops is approved for commercial sale, Miragen anticipates incurring significant costs associated with commercializing any approved product candidate. Portions of its current pipeline of product candidates have been in-licensed from third parties, which make the commercial sale of such in-licensed products potentially subject to additional royalty and milestone payments to such third-parties. Miragen will also have to develop or acquire manufacturing capabilities or continue to contract with contract manufacturers in order to continue development and potential commercialization of its product

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candidates. For instance, Miragen s current costs of manufacturing its drug product is not commercially feasible and it will need to develop or procure its drug product in a commercially feasible manner in order to successfully commercialize any future approved product, if any. Additionally, if Miragen is not able to generate revenue from the sale of any approved products, Miragen may never become profitable.

Raising additional capital may cause dilution to Miragen s stockholders, restrict its operations or require Miragen to relinquish rights.

To the extent that Miragen raises additional capital through the sale of equity, convertible debt or other securities convertible into equity, including the issuance of shares of capital stock in its concurrent financing in connection with the Merger, the ownership interest of Miragen s stockholders will be diluted, and the terms of these new securities may include liquidation or other preferences that adversely affect rights of Miragen s stockholders. Debt financing, if available at all, would likely involve agreements that include covenants limiting or restricting Miragen s ability to take specific actions, such as incurring additional debt, making capital expenditures, making additional product acquisitions, or declaring dividends. For instance, Miragen s loan and security agreement with Silicon Valley Bank limits Miragen s ability to enter into an asset sale, enter into any change of control, incur additional indebtedness, pay any dividends or enter into specified transactions with its affiliates. If Miragen raises additional funds through strategic collaborations or licensing arrangements with third parties, Miragen may have to relinquish valuable rights to its product candidates or future revenue streams or grant licenses on terms that are not favorable to Miragen. Miragen cannot be assured that it will be able to obtain additional funding if and when necessary to fund its entire portfolio of product candidates to meet its projected plans. If Miragen is unable to obtain funding on a timely basis, Miragen may be required to delay or discontinue one or more of its development programs or the commercialization of any product candidates or be unable to expand its operations or otherwise capitalize on potential business opportunities, which could materially harm Miragen s business, financial condition, and results of operations.

Miragen has also historically received funds from state and federal government grants for research and development. The grants have been, and any future government grants and contracts Miragen may receive may be, subject to the risks and contingencies set forth below under the risk factor titled *Reliance on government funding for Miragen s programs may add uncertainty to its research and commercialization efforts with respect to those programs that are tied to such funding and may impose requirements that limit its ability to take specified actions, increase the costs of commercialization and production of product candidates developed under those programs and subject it to potential financial penalties, which could materially and adversely affect its business, financial condition and results of operations*. Although Miragen might apply for government contracts and grants in the future, it cannot assure you that it will be successful in obtaining additional grants for any product candidates or programs.

Risks Related to the Development of Miragen s Product Candidates

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

Clinical development is expensive, time consuming and involves significant risk. Miragen cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical trials can occur at any stage of development. Events that may prevent successful or timely completion of clinical development include but are not limited to:

inability to generate satisfactory pre-clinical, toxicology, or other in vivo or in vitro data or diagnostics to support the initiation or continuation of clinical trials;

delays in reaching agreement on acceptable terms with clinical research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;

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delays in obtaining required institutional review board, or IRB, approval at each clinical trial site;

failure to permit the conduct of a clinical trial by regulatory authorities, after review of an investigational new drug or equivalent foreign application or amendment;

delays in recruiting qualified patients in its clinical trials;

failure by clinical sites or CROs or other third parties to adhere to clinical trial requirements;

failure by Miragen clinical sites, CROs or other third parties to perform in accordance with the good clinical practices requirements of the U.S. Food and Drug Administration, or the FDA, or applicable foreign regulatory guidelines;

patients dropping out of Miragen s clinical trials;

adverse events or tolerability or animal toxicology issues significant enough for the FDA or other regulatory agencies to put any or all clinical trials on hold;

occurrence of adverse events associated with Miragen s product candidates;

changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;

the cost of clinical trials of Miragen s product candidates;

negative or inconclusive results from Miragen s clinical trials which may result in Miragen s deciding, or regulators requiring Miragen, to conduct additional clinical trials or abandon development programs in other ongoing or planned indications for a product candidate; and

delays in reaching agreement on acceptable terms with third-party manufacturers and the time for manufacture of sufficient quantities of its product candidates for use in clinical trials.

Any inability to successfully complete clinical development and obtain regulatory approval for its product candidates could result in additional costs to Miragen or impair its ability to generate revenue. In addition, if Miragen makes manufacturing or formulation changes to its product candidates, Miragen may need to conduct additional pre-clinical trials or the results obtained from such new formulation may not be consistent with previous results obtained. Clinical trial delays could also shorten any periods during which its products have patent protection and may allow competitors to develop and bring products to market before Miragen does, which could impair its ability to successfully commercialize its product candidates and may harm its business and results of operations.

The approach Miragen is 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 Miragen s efforts to discover and develop its product candidates are relatively recent. To date, neither Miragen nor any other company has received regulatory approval to market therapeutics utilizing microRNA targeted molecules. The scientific evidence to support the feasibility of developing drugs based on these discoveries is both preliminary and limited. Successful development of microRNA therapeutic products by Miragen 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 product candidates that Miragen develops may not demonstrate in patients the chemical and pharmacological properties ascribed to them in laboratory and pre-clinical trials, and they may interact with human biological systems in unforeseen, ineffective or even harmful ways. For instance, Miragen s clinical and pre-clinical data to date is not validated and Miragen has no way of knowing if after validation Miragen s clinical trial data will be complete and consistent. If Miragen does not successfully develop and commercialize product candidates based upon this technological approach, it may not become profitable and the value of its capital stock may decline.

Further, Miragen s focus on microRNA technology for developing product candidates as opposed to multiple, more proven technologies for drug development increases the risk associated with its business. If Miragen is not

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successful in developing an approved product using microRNA technology, it may not be able to identify and successfully implement an alternative product development strategy. In addition, work by other companies pursuing similar technologies may encounter setbacks and difficulties that regulators and investors may attribute to Miragen s product candidates, whether appropriate or not.

Miragen s 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 in the United States.

Miragen has concentrated its research and development efforts to date on a limited number of product candidates based on its microRNA therapeutic platform and identifying its initial targeted disease indications. Miragen s future success depends on its successful development of viable product candidates. Currently, only two of its product candidates, MRG-106 and MRG-201, are in clinical development, and the remainder of its product candidates are in pre-clinical development. There can be no assurance that Miragen will not experience problems or delays in developing its product candidates and that such problems or delays will not cause unanticipated costs, or that any such development problems can be solved.

Additionally, the FDA has relatively limited experience with microRNA-targeted therapeutics. No regulatory authority has granted approval to any person or entity, including Miragen, to market or commercialize microRNA therapeutics, which may increase the complexity, uncertainty and length of the regulatory approval process for Miragen s product candidates. If Miragen s microRNA product candidates fail to prove to be safe, effective or commercially viable, its product candidate pipeline would have little, if any, value, which would have a material adverse effect on its business, financial condition or results of operations.

The clinical trial and manufacturing requirements of the FDA, the European Medicines Agency, or the EMA, and other regulatory authorities, and the criteria these regulators use to determine the safety and efficacy of a product candidate, vary substantially according to the type, complexity, novelty and intended use and market of the product candidate. The regulatory approval process for novel product candidates such as microRNA therapeutics can be more expensive and take longer than for other, better known or more extensively studied product candidates. It is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for Miragen s product candidates in either the United States or the European Union or how long it will take to commercialize its product candidates, even if approved for marketing. Approvals by the European Commission may not be indicative of what the FDA, and vice versa, may require for approval and different or additional pre-clinical trials or clinical trials may be required to support regulatory approval in each respective jurisdiction. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product candidate to market could decrease Miragen s ability to generate sufficient product revenue, and Miragen s business, financial condition, results of operations and prospects may be harmed.

Miragen may not be able to develop or identify a technology that can effectively deliver MRG-106, MRG-201 or any other of its microRNA-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 its other product candidates.

In connection with its Phase 1 clinical trials of MRG-106 and MRG-201, Miragen has used subcutaneous and intradermal injections as the route of product candidate administration. Miragen cannot be certain that subcutaneous or intradermal injections will be capable of delivering adequate levels of MRG-106, MRG-201 or its other product candidates to produce a therapeutic response for all indications. While Miragen is continuing to evaluate the use of subcutaneous, intraveneous and intradermal injections in different indications, and additional delivery technologies

and routes of administration that might enable it to target specific cells with its product candidates, Miragen cannot be certain whether it will be successful in developing such alternative delivery mechanisms. Miragen s failure to effectively deliver any of its product candidates to the intended diseased cells or tissues could adversely affect and delay the development of its product candidates.

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

Undesirable side effects caused by its product candidates could cause Miragen or regulatory authorities to interrupt, delay, or terminate clinical trials or even if approved, result in a restrictive label or delay regulatory approval by the FDA or comparable foreign authorities.

In addition, Miragen s MRG-106 and MRG-201 product candidates have been studied in only a limited number of patients with a confirmed diagnosis of MF and healthy volunteers, respectfully, and the most common adverse events of any grade were injection site reactions, including pain, itchiness and swelling. Miragen may experience a higher rate or severity of adverse events and comparable or higher rates of discontinuation in testing in its future clinical trials. There is no guarantee that additional or more severe side effects will not be identified through ongoing clinical trials of Miragen s product candidates for current and other indications. Undesirable side effects and negative results for other indications may negatively impact the development and potential for approval of Miragen s product candidates for their proposed indications.

Additionally, even if one or more of its product candidates receives marketing approval, and Miragen or others later identify undesirable side effects caused by such products, potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may withdraw approvals of such products;
- regulatory authorities may require additional warnings on the label;
- Miragen may be required to create a Risk Evaluation and Mitigation Strategy, or REMS, plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers, and/or other elements to assure safe use;
- Miragen could be sued and held liable for harm caused to patients; and
- its reputation may suffer.

Any of these events could prevent Miragen from achieving or maintaining market acceptance of a product candidate, even if approved, and could significantly harm its business, results of operations, and prospects.

Miragen s product development program may not uncover all possible adverse events that patients who take MRG-106, MRG-201 or its other product candidates may experience. The number of subjects exposed to MRG-106, MRG-201 or its 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, Miragen cannot be fully assured that rare and severe side effects of MRG-106, MRG-201 or its 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 MRG-106, MRG-201 or another product candidate reaches the market, the FDA may require that Miragen amend the labeling of the product or recall the product, or may even withdraw approval for the product.

Miragen s microRNA therapeutic approach is novel. Negative public opinion and increased regulatory scrutiny of microRNA or other nucleic acid based therapies may damage public perception of the safety of its product candidates and adversely affect its ability to conduct its business or obtain regulatory approvals for its product candidates.

MicroRNA therapy remains a novel technology, with no microRNA therapy product approved to date in the United States. Public perception may be influenced by claims that microRNA therapy is unsafe, and microRNA

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therapy may not gain the acceptance of the public or the medical community. In particular, Miragen s success will depend upon physicians who specialize in the treatment of the diseases targeted by Miragen s product candidates, prescribing treatments that involve the use of its product candidates in lieu of, or in addition to, existing treatments with which they are familiar and for which greater clinical data may be available. More restrictive government regulations or negative public opinion regarding microRNA or other nucleic acid based therapeutics could have an adverse effect on Miragen s business, financial condition or results of operations and may delay or impair the development and commercialization of its product candidates or demand for any products Miragen may develop. Serious adverse events in microRNA clinical trials for Miragen s competitors products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity, could result in increased government regulation, unfavorable public perception, potential regulatory delays in the testing or approval of Miragen s product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. For instance, in June 2016, the FDA placed a regulatory hold on the clinical trial of a microRNA or nucleic acid focused biopharmaceutical company with a microRNA product candidate for the treatment of hepatitis C virus due to serious adverse events in that trial. Another microRNA-focused biopharmaceutical company also voluntarily halted an ongoing Phase 1 trial for a microRNA therapy for multiple cancers in September 2016 due to multiple immune-related severe adverse events. Miragen cannot predict what effect, if any, these clinical holds will have on the government and public perception of Miragen s product candidates.

Miragen is heavily dependent on the success of its product candidates, which are in the early stages of clinical development. Some of its product candidates have produced results in pre-clinical settings to date, or for other indications than those for which Miragen contemplates conducting development and seeking FDA approval, and Miragen cannot give any assurance that it will generate data for any of its product candidates sufficient to receive regulatory approval in its planned indications, which will be required before they can be commercialized.

Miragen has invested substantially all of its efforts and financial resources to identify, acquire and develop its portfolio of product candidates. Its future success is dependent on its ability to successfully further develop, obtain regulatory approval for, and commercialize one or more product candidates. Miragen currently generates no revenue from sales of any products, and Miragen may never be able to develop or commercialize a product candidate.

Miragen currently has two product candidates in Phase 1 clinical trials. Of these Miragen product candidates, MRG-106 has only been administered in volunteers with MF. This is only one of the multiple indications for which Miragen plans to develop this product candidate. Additionally, Miragen s clinical and pre-clinical data to date is not validated and Miragen has no way of knowing if after validation Miragen s clinical trial data will be complete and consistent. There can be no assurance that the data that Miragen develops for its product candidates in its planned indications will be sufficient to obtain regulatory approval.

In addition, none of its product candidates have advanced into a pivotal clinical trial for Miragen s proposed indications and it may be years before any such clinical trial is initiated and completed, if at all. Miragen is not permitted to market or promote any of its product candidates before it receives regulatory approval from the FDA or comparable foreign regulatory authorities, and Miragen may never receive such regulatory approval for any of its product candidates. Miragen cannot be certain that any of its product candidates will be successful in clinical trials or receive regulatory approval. Further, its product candidates may not receive regulatory approval even if they are successful in clinical trials. If Miragen does not receive regulatory approvals for its product candidates, Miragen may not be able to continue its operations.

Product development involves a lengthy and expensive process with an uncertain outcome, and results of earlier pre-clinical and clinical trials may not be predictive of future clinical trial results.

Clinical testing is expensive and generally takes many years to complete, and the outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of pre-clinical trials and early

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clinical trials of Miragen s product candidates may not be predictive of the results of larger, later-stage controlled clinical trials. Product candidates that have shown promising results in early-stage clinical trials may still suffer significant setbacks in subsequent clinical trials. Miragen s clinical trials to date have been conducted on a small number of patients in limited numbers of clinical sites for a limited number of indications. Miragen will have to conduct larger, well-controlled trials in its proposed indications to verify the results obtained to date and to support any regulatory submissions for further clinical development. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles despite promising results in earlier, smaller clinical trials. For instance, in June 2016, the FDA placed a regulatory hold on the clinical trial of a microRNA-focused biopharmaceutical company with a microRNA product candidate for the treatment of hepatitis C virus due to serious adverse events in that trial. Another microRNA-focused biopharmaceutical company also voluntarily halted an ongoing Phase 1 trial for a microRNA therapy for multiple cancers in September 2016 due to multiple immune-related severe adverse events. Moreover, clinical data are often susceptible to varying interpretations and analyses. Miragen does not know whether any Phase 2, Phase 3, or other clinical trials Miragen may conduct will demonstrate consistent or adequate efficacy and safety with respect to the proposed indication for use sufficient to receive regulatory approval or market its drug candidates.

Miragen may use its 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 Miragen has limited financial and human resources, it may forego or delay pursuit of opportunities with some programs or product candidates or for other indications that later prove to have greater commercial potential. Miragen s resource allocation decisions may cause it to fail to capitalize on viable commercial products or more profitable market opportunities. Miragen s spending on current and future research and development programs and future product candidates for specific indications may not yield any commercially viable products. Miragen may also enter into additional strategic collaboration agreements to develop and commercialize some of its programs and potential product candidates in indications with potentially large commercial markets. If Miragen does not accurately evaluate the commercial potential or target market for a particular product candidate, it may relinquish valuable rights to that product candidate through strategic collaborations, licensing or other royalty arrangements in cases in which it would have been more advantageous for Miragen to retain sole development and commercialization rights to such product candidate, or Miragen 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.

Miragen may find it difficult to enroll patients in its clinical trials given the limited number of patients who have the diseases for which its product candidates are being studied. Difficulty in enrolling patients could delay or prevent clinical trials of its product candidates.

Identifying and qualifying patients to participate in clinical trials of Miragen s product candidates is essential to its success. The timing of Miragen s clinical trials depends in part on the rate at which Miragen can recruit patients to participate in clinical trials of its product candidates, and Miragen may experience delays in its clinical trials if Miragen encounters difficulties in enrollment.

The eligibility criteria of Miragen s planned clinical trials may further limit the available eligible trial participants as Miragen expects to require that patients have specific characteristics that Miragen can measure or meet the criteria to assure their conditions are appropriate for inclusion in its clinical trials. For instance, Miragen s Phase 1 clinical trial of MRG-106 includes patients with MF. The estimated prevalence of MF is 16,000 to 20,000 cases in the United States and only a subset of this group satisfies the enrollment criteria for Miragen s MRG-106 clinical trial. Miragen may not be able to identify, recruit, and enroll a sufficient number of patients to complete its clinical trials in a timely manner

because of the perceived risks and benefits of the product candidate under study, the availability and efficacy of competing therapies and clinical trials, and the

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willingness of physicians to participate in its planned clinical trials. If patients are unwilling to participate in Miragen s clinical trials for any reason, the timeline for conducting trials and obtaining regulatory approval of its product candidates may be delayed.

If Miragen experiences delays in the completion of, or termination of, any clinical trials of its product candidates, the commercial prospects of its product candidates could be harmed, and its ability to generate product revenue from any of these product candidates could be delayed or prevented. In addition, any delays in completing its clinical trials would likely increase its overall costs, impair product candidate development and jeopardize its ability to obtain regulatory approval relative to its current plans. Any of these occurrences may harm its business, financial condition, and prospects significantly.

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

The use or misuse of Miragen s product candidates in clinical trials and the sale of any products for which Miragen may obtain marketing approval exposes Miragen to the risk of potential product liability claims. Product liability claims might be brought against Miragen by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with its product candidates and approved products, if any. There is a risk that Miragen s product candidates may induce adverse events. If Miragen cannot successfully defend against product liability claims, it could incur substantial liability and costs. Some of its microRNA therapeutics have shown in clinical trials adverse events, including injection site reactions and pain at the injection site, nausea, decreased white blood cell count, neutropenia, elevated aspartate aminotransferase, alanine aminotransferase and creatine kinase levels, prolonged partial thromboplastin time, blurred vision, itchiness, fatigue, headache and microscopic hematuria, among others. There is a risk that Miragen s future product candidates may induce similar or more severe adverse events. Patients with the diseases targeted by Miragen s product candidates may already be in severe and advanced stages of disease and have both known and unknown significant preexisting 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 Miragen s product candidates. Such events could subject Miragen to costly litigation, require it to pay substantial amounts of money to injured patients, delay, negatively impact or end its opportunity to receive or maintain regulatory approval to market its products, or require Miragen to suspend or abandon its commercialization efforts. Even in a circumstance in which an adverse event is unrelated to Miragen s product candidates, the investigation into the circumstance may be time-consuming or inconclusive. These investigations may delay Miragen s regulatory approval process or impact and limit the type of regulatory approvals its 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 Miragen s business, financial condition or results of operations.

Although Miragen has product liability insurance, which covers its clinical trials in the United States, for up to $5.0 million per occurrence, up to an aggregate limit of $5.0 million, its insurance may be insufficient to reimburse it for any expenses or losses Miragen may suffer. Miragen will also likely be required to increase its product liability insurance coverage for the advanced clinical trials that it plans to initiate. If Miragen obtains marketing approval for any of its product candidates, it will need to expand its insurance coverage to include the sale of commercial products. There is no way to know if Miragen will be able to continue to obtain product liability coverage and obtain expanded coverage if it requires it, in sufficient amounts to protect it against losses due to liability, on acceptable terms, or at all.

Miragen may not have sufficient resources to pay for any liabilities resulting from a claim excluded from, or beyond the limits of, its insurance coverage. Where Miragen has provided indemnities in favor of third parties under its agreements with them, there is also a risk that these third

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parties could incur liability and bring a claim under such indemnities. An individual may bring a product liability claim against Miragen alleging that one of its product candidates 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 Miragen, 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, its product candidates;
- if commercialized, product recalls, withdrawals of 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 Miragen s product liability insurance, which Miragen would then be required to pay itself;
- an increase in Miragen s 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 Miragen s business; and
- damage to Miragen s reputation and the reputation of its products and its technology.

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

Risks Related to Regulatory Approval of Miragen s Product Candidates and Other Legal Compliance Matters

A potential breakthrough therapy designation by the FDA for Miragen s product candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that Miragen s

product candidates will receive marketing approval.

Miragen may seek a breakthrough therapy designation from the FDA for some of its product candidates. A breakthrough therapy is defined as a drug or biological product that 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 or biological product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs or biological products that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA could also be eligible for accelerated approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if Miragen believes one of its product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of Miragen s product candidates qualify and are designated as breakthrough therapies, the FDA may later decide that the drugs or biological products no longer meet the conditions for designation and the designation may be rescinded.

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Miragen may seek Fast Track designation for one or more of its product candidates, but it might not receive such designation, and even if Miragen does, such designation may not actually lead to a faster development or regulatory review or approval process.

If a product candidate is intended for the treatment of a serious condition and nonclinical or clinical data demonstrate the potential to address unmet medical need for this condition, a product sponsor may apply for FDA Fast Track designation. If Miragen seeks Fast Track designation for a product candidate, Miragen may not receive it from the FDA. However, even if Miragen receives Fast Track designation, Fast Track designation does not ensure that Miragen will receive marketing approval or that approval will be granted within any particular timeframe. Miragen may not experience a faster development or regulatory review or approval process with Fast Track designation compared to conventional FDA procedures. In addition, the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from Miragen s clinical development program. Fast Track designation alone does not guarantee qualification for the FDA s priority review procedures.

Even if Miragen obtains regulatory approval for a product, Miragen will remain subject to ongoing regulatory requirements.

If any of Miragen s product candidates are approved, Miragen will be subject to ongoing regulatory requirements with respect to manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing clinical trials, and submission of safety, efficacy and other post-approval information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturers facilities are required to continuously comply with FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to current Good Manufacturing Practices, or cGMP, regulations and corresponding foreign regulatory manufacturing requirements. As such, Miragen and its contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA or marketing authorization application.

Any regulatory approvals that Miragen receives for its product candidates may be subject to limitations on the approved indicated uses for which the product candidate may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. Miragen will be required to report adverse reactions and production problems, if any, to the FDA and comparable foreign regulatory authorities. Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. If its original marketing approval for a product candidate was obtained through an accelerated approval pathway, Miragen could be required to conduct a successful post-marketing clinical trial in order to confirm the clinical benefit for its products. An unsuccessful post-marketing clinical trial or failure to complete such a trial could result in the withdrawal of marketing approval.

If a regulatory agency 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, or disagrees with the promotion, marketing or labeling of a product, the regulatory agency may impose restrictions on that product or Miragen, including requiring withdrawal of the product from the market. If Miragen fails to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

issue warning letters;

impose civil or criminal penalties;

suspend or withdraw regulatory approval;

suspend any of Miragen s ongoing clinical trials;

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refuse to approve pending applications or supplements to approved applications submitted by Miragen;

impose restrictions on Miragen s operations, including closing its contract manufacturers facilities; or

require a product recall.

Any government investigation of alleged violations of law would be expected to require Miragen to expend significant time and resources in response and could generate adverse publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect its ability to develop and commercialize its products and the value of Miragen and its operating results would be adversely affected.

Healthcare legislative reform measures may have a material adverse effect on Miragen s business, financial condition or results of operations.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the Health Care Reform Law, was passed, which substantially changes the way health care is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The Health Care Reform Law, among other things, 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, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of specified branded prescription drugs, and promotes a new Medicare Part D coverage gap discount program.

In addition, other legislative changes have been proposed and adopted in the United States since the Health Care Reform Law was enacted and Miragen expects that additional state and federal healthcare reform measures 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 or lower pricing for its product candidates, or additional pricing pressures.

Miragen may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, and health information privacy and security laws. If Miragen is unable to comply, or has not fully complied, with such laws, it could face substantial penalties.

If Miragen obtains FDA approval for any of its product candidates and begins commercializing those products in the United States, its operations may be subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and physician sunshine laws and regulations. These laws may impact, among other things, its proposed sales, marketing, and education programs. In addition, Miragen may be subject to patient privacy regulation by both the federal government and the states in which Miragen conduct its business. The laws that may affect its ability to operate include:

the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program,

such as the Medicare and Medicaid programs;

federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;

the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;

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HIPAA, as amended by the Health Information Technology and Clinical Health Act, and its implementing regulations, which imposes specified requirements relating to the privacy, security, and transmission of individually identifiable health information;

the federal physician sunshine requirements under the Health Care Reform Laws requires manufacturers of drugs, devices, biologics, and medical supplies to report annually to the U.S. Department of Health and Human Services information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations; and

state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws that may apply to items or services reimbursed by any third-party payor, including governmental and private payors, to comply with the pharmaceutical industry s voluntary compliance guidelines and the relevant 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 specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of Miragen s business activities could be subject to challenge under one or more of such laws. In addition, recent health care reform legislation has strengthened these laws. For example, the Health Care Reform Law, among other things, amends the intent requirement of the federal anti-kickback and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. Moreover, the Health Care Reform Law provides that 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.

If Miragen s operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to Miragen, Miragen 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 its operations, any of which could adversely affect its ability to operate Miragen s business and its results of operations.

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

During the course of Miragen s development of its product candidates, it has been funded in part through federal and state grants, including but not limited to the funding it received from Yale University, or Yale, pursuant to a subcontract agreement with Yale. In addition to the funding Miragen has received to date, it has applied and intends 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 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 specified cases with interest, in the event Miragen violates specified covenants pertaining to various matters that include a failure to achieve

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specified milestones or to comply with terms relating to use of grant proceeds, or failure to comply with specified 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 Miragen may receive could also impose requirements to make payments based upon sales of its products, if any, in the future.

Miragen may not have the right to prohibit the U.S. government from using specified technologies developed by it, and Miragen may not be able to prohibit third-party companies, including its 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 Miragen licenses now or in the future.

In addition, government contracts and grants normally contain additional requirements that may increase Miragen s costs of doing business, reduce its profits, and expose it 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 some contract and grant information, which may enable competitors to gain insights into Miragen s research program; and
- mandatory socioeconomic compliance requirements, including labor standards, non-discrimination and affirmative action programs and environmental compliance requirements.

If Miragen fails to maintain compliance with any such requirements that may apply to it now or in the future, Miragen may be subject to potential liability and to termination of Miragen s contracts.

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If Miragen fails to comply with environmental, health and safety laws and regulations, Miragen could become subject to fines or penalties or incur costs that could have a material adverse effect on its business, financial condition or results of operations.

Miragen s research and development activities and its third-party manufacturers and suppliers activities involve the controlled storage, use, and disposal of hazardous materials, including the components of its product candidates and other hazardous compounds. Miragen and its manufacturers and suppliers are subject to laws and regulations governing the use, manufacture, storage, handling, and disposal of these hazardous materials. In some cases, these hazardous materials and various wastes resulting from their use are stored at Miragen s and its manufacturers facilities pending their use and disposal. Miragen cannot eliminate the risk of contamination, which could cause an interruption of its commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products. Although Miragen believes that the safety procedures utilized by it and its third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, Miragen cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, Miragen may be held liable for any resulting damages and such liability could exceed its resources and state or federal or other applicable authorities may curtail Miragen s use of specified materials and/or interrupt its business operations. Furthermore, environmental laws and regulations are complex, change frequently, and have tended to become more stringent. Miragen cannot predict the impact of such changes and cannot be certain of its future compliance. Miragen does not currently carry biological or hazardous waste insurance coverage.

Risks Related to Miragen s Intellectual Property

Miragen may not be successful in obtaining or maintaining necessary rights to microRNA targets, product compounds and processes for its development pipeline through acquisitions and in-licenses.

Presently, Miragen has rights to the intellectual property, through licenses from third parties and under patents and patent applications that Miragen owns, to modulate only a subset of the known microRNA targets. Because Miragen s programs may involve a range of microRNA targets, including targets that require the use of proprietary rights held by third parties, the growth of its business will likely depend in part on Miragen s ability to acquire, in-license or use these proprietary rights. In addition, Miragen s product candidates may require specific formulations to work effectively and efficiently and these rights may be held by others. Miragen may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that it identifies. 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 Miragen may consider attractive. These established companies may have a competitive advantage over Miragen due to their size, cash resources and greater clinical development and commercialization capabilities.

For example, Miragen has previously and may continue to collaborate with U.S. and foreign academic institutions to accelerate its pre-clinical research or development under written agreements with these institutions. Typically, these institutions provide an option to negotiate a license to any of the institution s rights in technology resulting from the collaboration. Regardless of such right of first negotiation for intellectual property, Miragen may be unable to negotiate a license within the specified time frame or under terms that are acceptable to it. If Miragen is unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking Miragen s ability to pursue its program.

In addition, companies that perceive Miragen to be a competitor may be unwilling to assign or license rights to it. Miragen also may be unable to license or acquire third-party intellectual property rights on terms that would allow it to make an appropriate return on its investment. If Miragen is unable to successfully obtain rights to third-party intellectual property rights, its business, financial condition and prospects for growth could suffer.

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Miragen intends to rely on patent rights for its product candidates and any future product candidates. If Miragen is unable to obtain or maintain exclusivity from the combination of these approaches, Miragen may not be able to compete effectively in its markets.

Miragen relies or will rely upon a combination of patents, trade secret protection, and confidentiality agreements to protect the intellectual property related to its technologies and product candidates. Its success depends in large part on its and its licensors ability to obtain regulatory exclusivity and maintain patent and other intellectual property protection in the United States and in other countries with respect to its proprietary technology and products.

Miragen has sought to protect its proprietary position by filing patent applications in the United States and abroad related to its product candidates that are important to its business. This process is expensive and time consuming, and Miragen may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that Miragen will fail to identify patentable aspects of its research and development output before it is too late to obtain patent protection.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain and involves complex legal and factual questions for which legal principles remain unsolved. The patent applications that Miragen owns or in-licenses may fail to result in issued patents with claims that cover its product candidates in the United States or in other foreign countries. There is no assurance that all potentially relevant prior art relating to its 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 do successfully issue, and even if such patents cover Miragen s product candidates, third parties may challenge their validity, enforceability, or scope, which may result in such patents being narrowed, found unenforceable or invalidated. Furthermore, even if they are unchallenged, Miragen s patents and patent applications may not adequately protect its intellectual property, provide exclusivity for its product candidates, or prevent others from designing around the Miragen claims. Any of these outcomes could impair Miragen s ability to prevent competition from third parties, which may have an adverse impact on its business.

Miragen, independently or together with its licensors, has filed several patent applications covering various aspects of its product candidates. Miragen cannot offer any assurances about which, if any, patents will issue, the breadth of any such patent or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful opposition to these patents or any other patents owned by or licensed to Miragen after patent issuance could deprive Miragen of rights necessary for the successful commercialization of any product candidates that Miragen may develop. Further, if Miragen encounters delays in regulatory approvals, the period of time during which Miragen could market a product candidate under patent protection could be reduced.

If Miragen cannot obtain and maintain effective protection of exclusivity from its regulatory efforts and intellectual property rights, including patent protection or data exclusivity, for its product candidates, Miragen may not be able to compete effectively and its business and results of operations would be harmed.

Miragen may not have sufficient patent term protections for its product candidates to effectively protect its business.

Patents have a limited term. In the United States, the statutory expiration of a patent is generally 20 years after it is filed. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Even if patents covering its product candidates are obtained, once the patent life has expired for a product candidate, Miragen may be open to competition from generic medications. In addition, upon issuance in the United States any patent term can be adjusted based on specified delays caused by the applicant(s) or the USPTO.

Patent term extensions under the Hatch-Waxman Act in the United States and under supplementary protection certificates in Europe may be available to extend the patent or data exclusivity terms of Miragen s product

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candidates. Miragen will likely rely on patent term extensions, and Miragen cannot provide any assurances that any such patent term extensions will be obtained and, if so, for how long. As a result, Miragen may not be able to maintain exclusivity for its product candidates for an extended period after regulatory approval, if any, which would negatively impact its business, financial condition, results of operations and prospects. If Miragen does not have sufficient patent terms or regulatory exclusivity to protect its product candidates, its business and results of operations will be adversely affected.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing Miragen s ability to protect its products, and recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of its patent applications and the enforcement or defense of its issued patents.

As is the case with other biotechnology companies, Miragen s 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 specified circumstances and weakened the rights of patent owners in specified situations. In addition to increasing uncertainty with regard to Miragen s 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 Miragen s ability to obtain new patents or to enforce Miragen s existing patents and patents that it might obtain in the future. Some of Miragen s 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.

On December 16, 2014, the USPTO issued guidance to patent examiners titled 2014 Interim Guidance on Patent Subject Matter Eligibility (Fed. Reg. 79 (241): 74618-33. These guidelines instruct USPTO examiners on the ramifications of the Prometheus and Myriad rulings and apply the Myriad ruling to natural products and principles including all naturally occurring nucleic acids. In addition, the USPTO continues to provide updates to its guidance and this is a developing area. The recent USPTO guidance could make it impossible for Miragen to pursue similar patent claims in patent applications Miragen may prosecute in the future.

Miragen s patent portfolio contains claims of various types and scope, including chemically modified mimics, as well as methods of medical treatment. The presence of varying claims in Miragen s patent portfolio significantly reduces, but may not eliminate, its 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 Miragen s business.

For Miragen s 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 Miragen s business. However, the Leahy-Smith

Act and its implementation could increase the uncertainties and costs surrounding the prosecution of its patent applications and the enforcement or defense of its issued patents, all of which could have a material adverse effect on Miragen s business, financial condition or results of operations.

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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 Miragen could therefore be awarded a patent covering an invention of Miragen s even if Miragen had made the invention before it was made by the third party. This will require Miragen to be cognizant going forward of the time from invention to filing of a patent application. Furthermore, Miragen s ability to obtain and maintain valid and enforceable patents depends on whether the differences between its technology and the prior art allow its 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, Miragen cannot be certain that it was the first to either (i) file any patent application related to its product candidates or (ii) invent any of the inventions claimed in its 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 new procedures providing opportunities for third parties to challenge any issued patent in the USPTO. Included in these new procedures is a process known as Inter Partes Review, or IPR, which has been generally used by many third parties over the past two years to invalidate patents. The IPR process is not limited to patents filed after the Leahy-Smith Act was enacted, and would therefore be available to a third party seeking to invalidate any of Miragen s 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 U.S. 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 Miragen s patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action.

If Miragen is unable to maintain effective proprietary rights for its product candidates or any future product candidates, Miragen may not be able to compete effectively in its proposed markets.

In addition to the protection afforded by patents, Miragen relies on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that Miragen elects not to patent, processes for which patents are difficult to enforce and any other elements of its product candidate 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. Miragen seeks to protect its proprietary technology and processes, in part, by entering into confidentiality agreements with its employees, consultants, scientific advisors, and contractors. Miragen also seeks to preserve the integrity and confidentiality of its data and trade secrets by maintaining physical security of its premises and physical and electronic security of its information technology systems. While Miragen has confidence in these individuals, organizations and systems, agreements or security measures may be breached, and Miragen may not have adequate remedies for any breach. In addition, its trade secrets may otherwise become known or be independently discovered by competitors.

Although Miragen expects all of its employees and consultants to assign their inventions to Miragen, and all of its employees, consultants, advisors, and any third parties who have access to its proprietary know-how, information, or technology to enter into confidentiality agreements, Miragen cannot provide any assurances that all such agreements have been duly executed or that its trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to its trade secrets or independently develop substantially equivalent information and techniques. Misappropriation or unauthorized disclosure of Miragen s trade secrets could impair its competitive position and may have a material adverse effect on its business, financial condition or results of operations. Additionally, if the steps taken to maintain its trade secrets are deemed inadequate, Miragen may have

insufficient recourse against third parties for misappropriating the trade secret.

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Third-party claims of intellectual property infringement may prevent or delay Miragen s development and commercialization efforts.

Miragen s commercial success depends in part on its ability to develop, manufacture, market and sell its product candidates and use its 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. Miragen is aware of U.S. and foreign patents and pending patent applications owned by third parties that cover therapeutic uses of microRNA replacements and inhibitors. Miragen is currently monitoring these patents and patent applications. Miragen 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, Miragen 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 its product candidates or technologies, Miragen may not be free to manufacture or market its product candidates, including MRG-106 or MRG-201, as planned, absent such a license, which may not be available to Miragen on commercially reasonable terms, or at all.

It is also possible that Miragen has failed to identify relevant third-party patents or applications. For example, applications filed before November 29, 2000 and 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 Miragen, to identify all third-party patent rights that may be relevant to its 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. Miragen 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 its technology. In addition, Miragen 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 Miragen may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by its activities. Additionally, pending patent applications that have been published can, subject to specified limitations, be later amended in a manner that could cover Miragen s technologies, its product candidates or the use of its product candidates.

There have been many lawsuits and other proceedings involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, and reexamination proceedings before the USPTO and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which Miragen is developing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that its product candidates may be subject to claims of infringement of the patent rights of third parties.

Parties making claims against Miragen may obtain injunctive or other equitable relief, which could effectively block its ability to further develop and commercialize one or more of its 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 its business. In the event of a successful claim of infringement against Miragen, Miragen may have to pay substantial damages, including treble damages and attorneys fees for willful infringement, pay royalties, redesign its infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

Miragen may not be successful in meeting its obligations under its existing license agreements necessary to maintain its product candidate licenses in effect. In addition, if required in order to commercialize its product candidates, Miragen may be unsuccessful in obtaining or maintaining necessary rights to its product candidates

through acquisitions and in-licenses.

Miragen currently has rights to the intellectual property, through licenses from third parties and under patents that Miragen does not own, to develop and commercialize its product candidates. Because its programs may

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require the use of proprietary rights held by third parties, the growth of its business will likely depend in part on its ability to maintain in effect these proprietary rights. Any termination of license agreements with third parties with respect to its product candidates would be expected to negatively impact its business prospects.

Miragen may be unable to acquire or in-license any compositions, methods of use, processes, or other third-party intellectual property rights from third parties that Miragen identifies as necessary for its product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that Miragen may consider attractive. These established companies may have a competitive advantage over Miragen due to their size, cash resources, and greater clinical development and commercialization capabilities. In addition, companies that perceive Miragen to be a competitor may be unwilling to assign or license rights to Miragen. Even if Miragen is able to license or acquire third-party intellectual property rights that are necessary for its product candidates, there can be no assurance that they will be available on favorable terms.

Miragen collaborates with U.S. and foreign academic institutions to identify product candidates, accelerate its research and conduct development. Typically, these institutions have provided Miragen with an option to negotiate an exclusive license to any of the institution s rights in the patents or other intellectual property resulting from the collaboration. Regardless of such option, Miragen may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to Miragen. If Miragen is unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking its ability to pursue a program of interest to Miragen.

If Miragen is unable to successfully obtain and maintain rights to required third-party intellectual property, Miragen may have to abandon development of that product candidate or pay additional amounts to the third-party, and its business and financial condition could suffer.

The patent protection and patent prosecution for some of Miragen s product candidates is dependent on third parties.

While Miragen normally seeks and gains the right to fully prosecute the patents relating to its product candidates, there may be times when patents relating to its product candidates are controlled by its licensors. For instance, this is the case with its agreement with Santaris Pharma A/S, which has changed its name to Roche Innovation Center Copenhagen A/S, or RICC, who is primarily responsible for the prosecution of patents and patent applications licensed to Miragen under the applicable agreement. If they or any of its future licensors fail to appropriately and broadly prosecute and maintain patent protection for patents covering any of its product candidates, its ability to develop and commercialize those product candidates may be adversely affected and Miragen may not be able to prevent competitors from making, using, importing, and selling competing products. In addition, even where Miragen now has the right to control patent prosecution of patents and patent applications Miragen has licensed from third parties, Miragen may still be adversely affected or prejudiced by actions or inactions of its licensors in effect from actions prior to Miragen assuming control over patent prosecution.

If Miragen fails to comply with obligations in the agreements under which Miragen licenses intellectual property and other rights from third parties or otherwise experience disruptions to its business relationships with its licensors, Miragen could lose license rights that are important to its business.

Miragen is a party to a number of intellectual property license and supply agreements that are important to its business and expects to enter into additional license agreements in the future. Miragen s existing agreements impose, and Miragen expects that future license agreements will impose, various diligence, milestone payment, royalty, purchasing, and other obligations on it. If Miragen fails to comply with its obligations under these agreements, or

Miragen is subject to a bankruptcy, its agreements may be subject to termination by the licensor, in which event Miragen would not be able to develop, manufacture, or market products covered by the license or subject to supply commitments.

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Miragen may be involved in lawsuits to protect or enforce its patents or the patents of its licensors, which could be expensive, time consuming, and unsuccessful.

Competitors may infringe Miragen s patents or the patents of its licensors. If Miragen or one of its licensing partners were to initiate legal proceedings against a third party to enforce a patent covering one of its product candidates, the defendant could counterclaim that the patent covering its product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, written description, clarity or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable.

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

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

Miragen may be subject to claims that its employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties or that its employees have wrongfully used or disclosed alleged trade secrets of their former employers.

Miragen employs individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including Miragen s competitors or potential competitors. Although Miragen has written agreements and makes every effort to ensure that its employees, consultants, and independent contractors do not use the proprietary information or intellectual property rights of others in their work for Miragen, Miragen may in the future be subject to any claims that its employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties. Litigation may be necessary to defend against these claims. If Miragen fails in defending any such claims, in addition to paying monetary damages, Miragen may lose valuable intellectual property rights or personnel, which could adversely impact its business. Even if Miragen is successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Miragen may not be able to protect its intellectual property rights throughout the world.

Filing, prosecuting, and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and its intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual

property rights to the same extent as federal and state laws in the United States. Competitors may use Miragen s technologies in jurisdictions where Miragen has not obtained patent protection to develop its own

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products and may also export infringing products to territories where Miragen has patent protection, but enforcement is not as strong as that in the United States. These products may compete with its products and its patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

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

Risks Related to Miragen s Reliance on Third Parties

Miragen relies on third parties to conduct its clinical trials, manufacture its product candidates and perform other services. If these third parties do not successfully perform and comply with regulatory requirements, Miragen may not be able to successfully complete clinical development, obtain regulatory approval or commercialize its product candidates and its business could be substantially harmed.

Miragen has relied upon and plans to continue to rely upon third-party CROs to conduct, monitor and manage its ongoing clinical programs. Miragen relies on these parties for execution of clinical trials and manages and controls only some aspects of their activities. Miragen remains responsible for ensuring that each of its trials is conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards and its reliance on the CROs does not relieve Miragen of its regulatory responsibilities. Miragen and its CROs and other vendors are required to comply with all applicable laws, regulations and guidelines, including those required by the FDA and comparable foreign regulatory authorities for all of its product candidates in clinical development. If Miragen or any of its CROs or vendors fail to comply with applicable laws, regulations and guidelines, the results generated in its clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require Miragen to perform additional clinical trials before approving its marketing applications. Miragen cannot be assured that its CROs and other vendors will meet these requirements, or that upon inspection by any regulatory authority, such regulatory authority will determine that efforts, including any of its clinical trials, comply with applicable requirements. Its failure to comply with these laws, regulations and guidelines may require Miragen to repeat clinical trials, which would be costly and delay the regulatory approval process.

If any of Miragen s relationships with these third-party CROs terminate, Miragen may not be able to enter into arrangements with alternative CROs in a timely manner or do so on commercially reasonable terms. In addition, Miragen s CROs may not prioritize Miragen s clinical trials relative to those of other customers and any turnover in personnel or delays in the allocation of CRO employees by the CRO may negatively affect its clinical trials. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, Miragen s clinical trials may be delayed or terminated and Miragen may not be able to meet its current plans with respect to its product candidates. CROs may also involve higher costs than anticipated, which could negatively affect Miragen s financial condition and operations.

In addition, Miragen does not currently have, nor does Miragen currently plan to establish the capability to manufacture product candidates for use in the conduct of its clinical trials, and Miragen lacks the resources and the capability to manufacture any of its product candidates on a clinical or commercial scale without the use of third-party manufacturers. Miragen plans to rely on third-party manufacturers and their responsibilities will

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include purchasing from third-party suppliers the materials necessary to produce its product candidates for its clinical trials and regulatory approval. There are expected to be a limited number of suppliers for the active ingredients and other materials that Miragen expects to use to manufacture its product candidates, and Miragen may not be able to identify alternative suppliers to prevent a possible disruption of the manufacture of its product candidates for its clinical trials, and, if approved, ultimately for commercial sale. Although Miragen generally does not expect to begin a clinical trial unless Miragen believes it has a sufficient supply of a product candidate to complete the trial, any significant delay or discontinuity in the supply of a product candidate, or the active ingredient or other material components in the manufacture of the product candidate could delay completion of its clinical trials and potential timing for regulatory approval of its product candidates, which would harm its business and results of operations.

Miragen relies and expects to continue to rely on third parties to manufacture its clinical product supplies, and Miragen intends to rely on third parties to produce and process its product candidates, if approved, and Miragen s commercialization of any of its product candidates could be stopped, delayed or made less profitable if those third parties fail to obtain approval of government regulators, fail to provide Miragen with sufficient quantities of drug product, or fail to do so at acceptable quality levels or prices.

Miragen does not currently have nor does it currently plan to develop the infrastructure or capability internally to manufacture its clinical supplies for use in the conduct of Miragen s clinical trials, and Miragen lacks the resources and the capability to manufacture any of its product candidates on a clinical or commercial scale. Miragen currently relies on outside vendors to manufacture its clinical supplies of its product candidates and plans to continue relying on third parties to manufacture its product candidates on a commercial scale, if approved.

Miragen does not yet have sufficient information to reliably estimate the cost of the commercial manufacturing of its product candidates and its current costs to manufacture its drug products is not commercially feasible, and the actual cost to manufacture its product candidates could materially and adversely affect the commercial viability of its product candidates. As a result, Miragen may never be able to develop a commercially viable product.

In addition, Miragen s reliance on third-party manufacturers exposes Miragen to the following additional risks:

- Miragen may be unable to identify manufacturers on acceptable terms or at all.
- Miragen s third-party manufacturers might be unable to timely formulate and manufacture Miragen s product or produce the quantity and quality required to meet Miragen s clinical and commercial needs, if any.
- Contract manufacturers may not be able to execute Miragen s manufacturing procedures appropriately.
- Miragen s future third-party manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to supply its clinical trials or to successfully produce, store and distribute its products.
- Manufacturers are subject to ongoing periodic unannounced inspection by the FDA and corresponding state agencies to ensure strict compliance with cGMPs and other government regulations and corresponding

foreign standards. Miragen does not have control over third-party manufacturers compliance with these regulations and standards.

Miragen may not own, or may have to share, the intellectual property rights to any improvements made by Miragen s third-party manufacturers in the manufacturing process for its product candidates.

Miragen s third-party manufacturers could breach or terminate their agreement with Miragen.

Each of these risks could delay Miragen s clinical trials, the approval, if any of its product candidates by the FDA or the commercialization of its product candidates or result in higher costs or deprive Miragen of potential

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product revenue. In addition, Miragen relies on third parties to perform release testing on its product candidates prior to delivery to patients. If these tests are not appropriately conducted and test data are not reliable, patients could be put at risk of serious harm and could result in product liability suits.

The manufacture of medical products is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of medical products often encounter difficulties in production, particularly in scaling up and validating initial production and absence of contamination. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, operator error, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. Furthermore, if contaminants are discovered in Miragen s supply of its product candidates or in the manufacturing facilities, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. Miragen cannot be assured that any stability or other issues relating to the manufacture of its product candidates will not occur in the future. Additionally, Miragen s manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If Miragen s manufacturers were to encounter any of these difficulties, or otherwise fail to comply with their contractual obligations, Miragen s ability to provide its product candidates to patients in clinical trials would be jeopardized. Any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require Miragen to commence new clinical trials at additional expense or terminate clinical trials completely.

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

Even if Miragen is 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 Miragen s share of potential future profits from the associated program, and may require it to relinquish potentially valuable rights to its current product candidates, potential products or proprietary technologies or grant licenses on terms that are not favorable to Miragen;

- collaborators may cease to devote resources to the development or commercialization of Miragen s product candidates if the collaborators view its 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 Miragen to litigation and potential liability;

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

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collaborations may be terminated and, if terminated, may result in a need for Miragen 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 Miragen s product candidates.

For instance, in October 2011, Miragen entered into a strategic alliance with Les Laboratoires Servier and the Institut de Recherches Servier, or Servier, for the research, development, and commercialization of RNA-targeting therapeutics in cardiovascular disease, or the Servier Collaboration Agreement, which was subsequently amended in May 2013, May 2014, May 2015 and September 2016. Under the Servier Collaboration Agreement, Miragen granted Servier an exclusive license to research, develop, and commercialize RNA-targeting therapeutics for three targets in the cardiovascular field. Servier s rights to each of the targets are limited to therapeutics in the cardiovascular field in their territory, which is worldwide except for the United States and Japan. Miragen retains all rights for each named target in the United States and Japan and for any products or product candidates outside of the cardiovascular field. Miragen cannot guarantee that any product candidate will ever be successfully commercialized under the Servier Collaboration Agreement. If no product candidate subject to the Servier Collaboration Agreement is successfully commercialized, Miragen may never receive additional milestone or any royalty payments under the Servier Collaboration Agreement. Also, due to restrictions contained in the Servier Collaboration Agreement, Miragen may not be able to effectively develop, market or commercialize any such product candidate in the United States and Japan.

Miragen enters into various contracts in the normal course of its business in which Miragen indemnifies the other party to the contract. In the event Miragen has to perform under these indemnification provisions, it could have a material adverse effect on its business, financial condition and results of operations.

In the normal course of business, Miragen periodically enters into academic, commercial, service, collaboration, licensing, consulting and other agreements that contain indemnification provisions. With respect to Miragen s academic and other research agreements, Miragen typically indemnifies the institution and related parties from losses arising from claims relating to the products, processes or services made, used, sold or performed pursuant to the agreements for which Miragen has secured licenses, and from claims arising from Miragen s or its sublicensees exercise of rights under the agreement. With respect to Miragen s collaboration agreements, Miragen indemnifies its collaborators from any third-party product liability claims that could result from the production, use or consumption of the product, as well as for alleged infringements of any patent or other intellectual property right by a third party. With respect to consultants, Miragen indemnifies them from claims arising from the good faith performance of their services.

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

Risks Related to Commercialization of Miragen s Product Candidates

Miragen currently has limited marketing and sales experience. If Miragen is unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell its product candidates, Miragen may be unable to generate any revenue.

Although some of its employees may have marketed, launched, and sold other pharmaceutical products in the past while employed at other companies, Miragen has no experience selling and marketing its product candidates

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and Miragen currently has no marketing or sales organization. To successfully commercialize any products that may result from its development programs, Miragen will need to find one or more collaborators to commercialize its products or invest in and develop these capabilities, either on its own or with others, which would be expensive, difficult and time consuming. Any failure or delay in the timely development of Miragen s internal commercialization capabilities could adversely impact the potential for success of its products.

If commercialization collaborators do not commit sufficient resources to commercialize its future products and Miragen is unable to develop the necessary marketing and sales capabilities on its own, Miragen will be unable to generate sufficient product revenue to sustain or grow its business. Miragen may be competing with companies that currently have extensive and well-funded marketing and sales operations, particularly in the markets its product candidates are intended to address. Without appropriate capabilities, whether directly or through third-party collaborators, Miragen may be unable to compete successfully against these more established companies.

Miragen may attempt to form collaborations in the future with respect to its product candidates, but it may not be able to do so, which may cause it to alter its development and commercialization plans.

Miragen may attempt to form strategic collaborations, create joint ventures or enter into licensing arrangements with third parties with respect to its programs that it believes will complement or augment its existing business. Miragen may face significant competition in seeking appropriate strategic collaborators, and the negotiation process to secure appropriate terms is time consuming and complex. Miragen may not be successful in its efforts to establish such a strategic collaboration for any product candidates and programs on terms that are acceptable to it, or at all. This may be because Miragen s product candidates and programs may be deemed to be at too early of a stage of development for collaborative effort, its 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 its 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 Miragen s product candidates could delay the development or commercialization of its product candidates, which may reduce their competitiveness even if they reach the market. Absent a strategic collaborator, Miragen would need to undertake development and/or commercialization activities at its own expense. If Miragen elects to fund and undertake development and/or commercialization activities on its own, it may need to obtain additional expertise and additional capital, which may not be available to it on acceptable terms or at all. If Miragen is unable to do so, it may not be able to develop its product candidates or bring them to market and its business may be materially and adversely affected.

If the market opportunities for its product candidates are smaller than Miragen believes they are, Miragen may not meet its revenue expectations and, assuming approval of a product candidate, its business may suffer. Because the patient populations in the market for its product candidates may be small, Miragen must be able to successfully identify patients and acquire a significant market share to achieve profitability and growth.

Given the small number of patients who have the diseases that Miragen is targeting, its eligible patient population and pricing estimates may differ significantly from the actual market addressable by its product candidates. For instance, Miragen s Phase 1 clinical trial in MRG-106 is focused on MF. The estimated prevalence of MF is 16,000 to 20,000 cases in the United States, only a subset of which may benefit from treatment with MRG-106. Miragen s projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with its product candidates, are based on its beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, patient foundations, or market research,

and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. Additionally, while Miragen believes that the data in its Phase 1 clinical trials for MRG-106 and

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MRG-201 are supportive of application to other indications, there can be no assurance that its clinical trials will successfully address any additional indications. Likewise, the potentially addressable patient population for each of its product candidates may be limited or may not be amenable to treatment with its product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect its business, financial condition, results of operations and prospects.

Miragen faces substantial competition and its competitors may discover, develop or commercialize products faster or more successfully than Miragen.

The development and commercialization of new drug products is highly competitive. Miragen faces competition from major pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies, universities and other research institutions worldwide with respect to MRG-106, MRG-201 and the other product candidates that it may seek to develop or commercialize in the future. Miragen is aware that the following companies have therapeutics marketed or in development for CTCL: Actelion Ltd, Bristol-Myers Squibb Company, Celgene Corporation, Merck & Co., Inc., Mylan Pharmaceuticals Inc., Novartis International AG, Spectrum Pharmaceuticals, Inc., Seattle Genetics, Inc., Takeda Pharmaceutical Company Ltd, and Valeant Pharmaceuticals International, Inc. Miragen is also aware that the several companies have marketed therapeutics for pulmonary fibrosis, including Boehringer Ingelheim GmbH and F. Hoffmann-La Roche Ltd. Miragen s competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective or less costly than MRG-106, MRG-201 or any other product candidates that Miragen is currently developing or that it may develop, which could render its product candidates obsolete and noncompetitive.

In addition to the competition Miragen faces from alternative therapies for the diseases it intends to target with its product candidates, Miragen is also aware of several companies that are also working specifically to develop microRNA therapeutics, including Mirna Therapeutics, Inc., Regulus Therapeutics, Inc., Microlin Bio, Inc. and InteRNA Technologies B.V. Further there are several companies working to develop other types of oligonucleotide therapeutic products, including Ionis Pharmaceuticals, Inc., Alnylam Pharmaceuticals, Inc., Dicerna Pharmaceuticals, Inc., RaNa Therapeutics, Inc., RXi Pharmaceuticals Corporation, and Silence Therapeutics AG. Many of Miragen s competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations. Third-party payors, including governmental and private insurers, may also encourage the use of generic products. For example, if MRG-106 or MRG-201 is approved, it may be priced at a significant premium over other competitive products. This may make it difficult for MRG-106, MRG-201 or any other future products to compete with these products.

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

Many of Miragen s competitors have materially greater name recognition and financial, manufacturing, marketing, research and drug development resources than it does. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in its competitors. Large pharmaceutical companies in particular have extensive expertise in pre-clinical 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 Miragen s competitors. Failure of MRG-106, MRG-201 or other product candidates to effectively compete against established treatment options or in the future with new products currently in development would harm Miragen s business, financial condition, results of operations and prospects.

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The commercial success of any of Miragen s current or future product candidates will depend upon the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community.

Even with the approvals from the FDA and comparable foreign regulatory authorities, the commercial success of Miragen s products will depend in part on the health care providers, patients, and third-party payors accepting its product candidates as medically useful, cost-effective, and safe. Any product that Miragen brings to the market may not gain market acceptance by physicians, patients and third-party payors. The degree of market acceptance of any of Miragen s products will depend on a number of factors, including but not limited to:

- the efficacy of the product as demonstrated in clinical trials and potential advantages over competing treatments;
- the prevalence and severity of the disease and any side effects;
- the clinical indications for which approval is granted, including any limitations or warnings contained in a product s approved labeling;
- the convenience and ease of administration;
- the cost of treatment;
- the willingness of the patients and physicians to accept these therapies;
- the perceived ratio of risk and benefit of these therapies by physicians and the willingness of physicians to recommend these therapies to patients based on such risks and benefits;
- the marketing, sales and distribution support for the product;
- the publicity concerning its products or competing products and treatments; and
- the pricing and availability of third-party insurance coverage and reimbursement.

Even if a product displays a favorable efficacy and safety profile upon approval, market acceptance of the product remains uncertain. Efforts to educate the medical community and third-party payors on the benefits of the products may require significant investment and resources and may never be successful. If its products fail to achieve an adequate level of acceptance by physicians, patients, third-party payors, and other health care providers, Miragen will not be able to generate sufficient revenue to become or remain profitable.

Miragen may not be successful in any efforts to identify, license, discover, develop, or commercialize additional product candidates.

Although a substantial amount of Miragen s effort will focus on the continued clinical testing, potential approval, and commercialization of its existing product candidates, the success of Miragen s business is also expected to depend in part upon its ability to identify, license, discover, develop, or commercialize additional product candidates. Research programs to identify new product candidates require substantial technical, financial, and human resources. Miragen may focus its efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. Miragen s research programs or licensing efforts may fail to yield additional product candidates for clinical development and commercialization for a number of reasons, including but not limited to the following:

Miragen s research or business development methodology or search criteria and process may be unsuccessful in identifying potential product candidates;

Miragen may not be able or willing to assemble sufficient resources to acquire or discover additional product candidates;

its product candidates may not succeed in pre-clinical or clinical testing;

its potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval;

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competitors may develop alternatives that render Miragen s product candidates obsolete or less attractive;

product candidates Miragen develops may be covered by third parties patents or other exclusive rights;

the market for a product candidate may change during Miragen s program so that such a product may become unreasonable to continue to develop;

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 any of these events occur, Miragen may be forced to abandon its development efforts for a program or programs, or Miragen may not be able to identify, license, discover, develop, or commercialize additional product candidates, which would have a material adverse effect on its business, financial condition or results of operations and could potentially cause Miragen to cease operations.

Failure to obtain or maintain adequate reimbursement or insurance coverage for products, if any, could limit Miragen s ability to market those products and decrease its ability to generate revenue.

The pricing, coverage, and reimbursement of Miragen s approved products, if any, must be sufficient to support its commercial efforts and other development programs and the availability and adequacy of coverage and reimbursement by third-party payors, including governmental and private insurers, are essential for most patients to be able to afford expensive treatments. Sales of Miragen s approved products, if any, will depend substantially, both domestically and abroad, on the extent to which the costs of its approved products, if any, will be paid for or reimbursed by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or government payors and private payors. If coverage and reimbursement are not available, or are available only in limited amounts, Miragen may have to subsidize or provide products for free or Miragen may not be able to successfully commercialize its products.

In addition, there is significant uncertainty related to the insurance coverage and reimbursement for newly approved products. In the United States, the principal decisions about coverage and reimbursement for new drugs are typically made by CMS, an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new drug will be covered and reimbursed under Medicare. Private payors tend to follow the coverage reimbursement policies established by CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for novel product candidates such as Miragen s and what reimbursement codes its product candidates may receive if approved.

Outside the United States, international operations are generally subject to extensive governmental price controls and other price-restrictive regulations, and Miragen believes the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries has and will continue to put pressure on the pricing and usage of products. In many countries, the prices of products are subject to varying price control mechanisms as part of national health systems. Price controls or other changes in pricing regulation could restrict the amount that Miragen is able to charge for its products, if any. Accordingly, in markets outside the United States, the potential revenue may be insufficient to

generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and private payors in the United States and abroad to limit or reduce healthcare costs may result in restrictions on coverage and the level of reimbursement for new products and, as a result, they may not cover or provide adequate payment for its products. Miragen expects to experience pricing pressures in connection with products due to the increasing trend toward managed healthcare, including the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs has and is expected to continue to increase

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in the future. As a result, profitability of Miragen s products, if any, may be more difficult to achieve even if they receive regulatory approval.

Risks Related to Miragen s Business Operations

Miragen s future success depends in part on its ability to retain its president and chief executive officer and to attract, retain, and motivate other qualified personnel.

Miragen is highly dependent on William S. Marshall, Ph.D., its president and chief executive officer, the loss of whose services may adversely impact the achievement of its objectives. Dr. Marshall could leave Miragen s employment at any time, as he is an at will employee. Recruiting and retaining other qualified employees, consultants, and advisors for Miragen s business, including scientific and technical personnel, will also be critical to Miragen success. There is currently a shortage of highly qualified personnel in Miragen s industry, which is likely to continue. Additionally, this shortage of highly qualified personnel is particularly acute in the area where Miragen is located. As a result, competition for personnel is intense and the turnover rate can be high. Miragen may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, failure to succeed in development and commercialization of Miragen s product candidates may make it more challenging to recruit and retain qualified personnel. The inability to recruit and retain qualified personnel, or the loss of the services of Dr. Marshall may impede the progress of Miragen s research, development, and commercialization objectives and would negatively impact Miragen s ability to succeed in its product development strategy.

Miragen will need to expand its organization and Miragen may experience difficulties in managing this growth, which could disrupt its operations.

As of December 31, 2016, Miragen had 43 full-time employees. As Miragen s development and commercialization plans and strategies develop, Miragen expects to need additional managerial, operational, sales, marketing, financial, legal, and other resources. Its management may need to divert a disproportionate amount of its attention away from its day-to-day activities and devote a substantial amount of time to managing these growth activities. Miragen may not be able to effectively manage the expansion of its operations, which may result in weaknesses in its infrastructure, operational mistakes, loss of business opportunities, loss of employees, and reduced productivity among remaining employees. Miragen s expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If its management is unable to effectively manage its growth, its expenses may increase more than expected, its ability to generate and/or grow revenue could be reduced and Miragen may not be able to implement its business strategy. Miragen s future financial performance and its ability to commercialize product candidates and compete effectively will depend, in part, on its ability to effectively manage any future growth.

Failure in Miragen s information technology and storage systems could significantly disrupt the operation of Miragen s business.

Miragen s ability to execute its business plan and maintain operations depends on the continued and uninterrupted performance of its information technology, or IT, systems. IT systems are vulnerable to risks and damages from a variety of sources, including telecommunications or network failures, malicious human acts and natural disasters. Moreover, despite network security and back-up measures, some of Miragen s and its vendors servers are potentially vulnerable to physical or electronic break-ins, including cyber-attacks, computer viruses and similar disruptive problems. These events could lead to the unauthorized access, disclosure and use of non-public information. The techniques used by criminal elements to attack computer systems are sophisticated, change frequently and may

originate from less regulated and remote areas of the world. As a result, Miragen may not be able to address these techniques proactively or implement adequate preventative measures. If its computer systems are compromised, it could be subject to fines, damages, litigation and enforcement actions, and it could

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lose trade secrets, the occurrence of which could harm its business. Despite precautionary measures to prevent unanticipated problems that could affect its IT systems, sustained or repeated system failures that interrupt Miragen s ability to generate and maintain data could adversely affect its ability to operate its business.

Miragen s principal stockholders own a significant percentage of its stock and will be able to exert significant control over matters subject to stockholder approval.

Miragen s principal stockholders and their affiliates currently beneficially own in excess of 76% of Miragen s outstanding voting stock, without giving effect to Miragen s concurrent financing in connection with the Merger. Therefore, these stockholders have the ability and may continue to have the ability to influence Miragen through this ownership position. These stockholders may be able to determine some or all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors, amendments of organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for Miragen s common stock that you may believe are in your best interest as one of Miragen s stockholders.

Risks Related to the Combined Company

In determining whether you should approve the Merger, the issuance of shares of Signal common stock and other matters related to the Merger, as applicable, you should carefully read the following risk factors in addition to the risks described above.

The market price of the combined company s common stock is expected to be volatile, and the market price of its common stock may drop following the Merger.

The market price of the combined company s common stock following the Merger could be subject to significant fluctuations. Market prices for securities of early-stage pharmaceutical, biotechnology and other life sciences companies have historically been particularly volatile. Some of the factors that may cause the market price of Signal s common stock to fluctuate include:

- the ability of the combined company to obtain regulatory approvals for MRG-106, MRG-201 or other product candidates, and delays or failures to obtain such approvals;
- failure of any of the combined company s product candidates, if approved, to achieve commercial success;
- failure to maintain its existing third-party license and supply agreements;
- failure by Signal or its licensors to prosecute, maintain, or enforce its intellectual property rights;
- changes in laws or regulations applicable to its product candidates;

any inability to obtain adequate supply of its product candidates or the inability to do so at acceptable prices;

adverse regulatory authority decisions;

introduction of new products, services, or technologies by its competitors;

failure to meet or exceed financial and development projections Miragen may provide to the public;

failure to meet or exceed the financial and development projections of the investment community;

the perception of the pharmaceutical industry by the public, legislatures, regulators, and the investment community;

announcements of significant acquisitions, strategic collaborations, joint ventures, or capital commitments by Signal or its competitors;

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disputes or other developments relating to proprietary rights, including patents, litigation matters, and its ability to obtain patent protection for its technologies;

additions or departures of key personnel;

significant lawsuits, including patent or stockholder litigation;

if securities or industry analysts do not publish research or reports about its business, or if they issue an adverse or misleading opinions regarding its business and stock;

changes in the market valuations of similar companies;

general market or macroeconomic conditions;

sales of its common stock by Signal or its stockholders in the future;

trading volume of its common stock;

announcements by commercial partners or competitors of new commercial products, clinical progress or the lack thereof, significant contracts, commercial relationships or capital commitments;

adverse publicity relating to microRNA therapeutics generally, including with respect to other products and potential products in such markets;

the introduction of technological innovations or new therapies that compete with potential products of the combined company;

changes in the structure of health care payment systems; and

period-to-period fluctuations in the combined company s financial results.

Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. These broad market fluctuations may also adversely affect the trading price of the combined company s common stock.

In the past, following periods of volatility in the market price of a company s securities, stockholders have often instituted class action securities litigation against those companies. Such litigation, if instituted, could result in

substantial costs and diversion of management attention and resources, which could significantly harm the combined company s profitability and reputation.

Additionally, a decrease in the stock price of the combined company may cause the combined company s common stock to no longer satisfy the continued listing standards of The NASDAQ Capital Market. If the combined company is not able to maintain the requirements for listing on The NASDAQ Capital Market, it could be delisted, which could have a materially adverse effect on its ability to raise additional funds as well as the price and liquidity of its common stock.

The combined company will incur costs and demands upon management as a result of complying with the laws and regulations affecting public companies.

The combined company will incur significant legal, accounting and other expenses that Miragen did not incur as a private company, including costs associated with public company reporting requirements. The combined company will also incur costs associated with corporate governance requirements, including requirements under the Sarbanes-Oxley Act, as well as new rules implemented by the SEC and The NASDAQ Stock Market LLC. These rules and regulations are expected to increase the combined company s legal and financial compliance costs and to make some activities more time-consuming and costly. For example, the combined company s management team will consist of the executive officers of Miragen prior to the Merger, some of whom have not previously managed and operated a public company. These executive officers and other personnel will need to devote substantial time to gaining expertise regarding operations as a public company and compliance with

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applicable laws and regulations. These rules and regulations may also make it difficult and expensive for the combined company to obtain directors and officers liability insurance. As a result, it may be more difficult for the combined company to attract and retain qualified individuals to serve on the combined company s board of directors or as executive officers of the combined company, which may adversely affect investor confidence in the combined company and could cause the combined company s business or stock price to suffer.

Anti-takeover provisions in the combined company s charter documents and under Delaware law could make an acquisition of the combined company more difficult and may prevent attempts by the combined company stockholders to replace or remove the combined company management.

Provisions in the combined company s certificate of incorporation and bylaws may delay or prevent an acquisition or a change in management. These provisions include a prohibition on actions by written consent of the combined company s stockholders, assuming that the Signal stockholders approve Signal Proposal No. 10, and the ability of the board of directors to issue preferred stock without stockholder approval. In addition, because the combined company will be incorporated in Delaware, it is governed by the provisions of Section 203 of the Delaware General Corporate Law, which prohibits stockholders owning in excess of 15% of the outstanding combined company voting stock from merging or combining with the combined company. Although Signal and Miragen believe these provisions collectively will provide for an opportunity to receive higher bids by requiring potential acquirors to negotiate with the combined company s board of directors, they would apply even if the offer may be considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by the combined company s stockholders to replace or remove then current management by making it more difficult for stockholders to replace members of the board of directors, which is responsible for appointing the members of management.

The bylaws of the combined company will provide that the Court of Chancery of the State of Delaware is the exclusive forum for substantially all disputes between the combined company and its stockholders, which could limit its stockholders ability to obtain a favorable judicial forum for disputes with the combined company or its directors, officers or other employees.

The bylaws of the combined company will provide that the Court of Chancery of the State of Delaware is the sole and exclusive forum for any derivative action or proceeding brought on the combined company s behalf, any action asserting a breach of fiduciary duty owed by any of its directors, officers or other employees to the combined company or its stockholders, any action asserting a claim against it arising pursuant to any provisions of the Delaware General Corporation Law, its certificate of incorporation or its bylaws, or any action asserting a claim against it that is governed by the internal affairs doctrine. The choice of forum provision may limit a stockholder s ability to bring a claim in a judicial forum that it finds favorable for disputes with the combined company or its directors, officers or other employees, which may discourage such lawsuits against the combined company and its directors, officers and other employees. If a court were to find the choice of forum provision contained in the bylaws to be inapplicable or unenforceable in an action, the combined company may incur additional costs associated with resolving such action in other jurisdictions.

Signal and Miragen do not anticipate that the combined company will pay any cash dividends in the foreseeable future.

The current expectation is that the combined company will retain its future earnings, if any, to fund the development and growth of the combined company s business. As a result, capital appreciation, if any, of the common stock of the combined company will be your sole source of gain, if any, for the foreseeable future.

An active trading market for the combined company s common stock may not develop and its stockholders may not be able to resell their shares of common stock for a profit, if at all.

Prior to the Merger, there had been no public market for Miragen s common stock. An active trading market for the combined company s shares of common stock may never develop or be sustained. If an active market for its

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common stock does not develop or is not sustained, it may be difficult for its stockholders to sell their shares at an attractive price or at all.

Future sales of shares by existing stockholders could cause the combined company s stock price to decline.

If existing stockholders of Signal and Miragen sell, or indicate an intention to sell, substantial amounts of the combined company s common stock in the public market after legal restrictions on resale discussed in this proxy statement/prospectus/information statement lapse, the trading price of the common stock of the combined company could decline. Based on shares outstanding as of December 31, 2016, shares expected to be issued upon completion of the Merger, and assuming completion of Miragen s concurrent financing in connection with the Merger, the combined company is expected to have outstanding a total of approximately 21.2 million shares of common stock immediately following the completion of the Merger, assuming an Exchange Ratio of 0.6995, without giving effect to the reverse stock split. Of the 21.2 million shares of common stock, 13.6 million shares, assuming an Exchange Ratio of 0.6995, without giving effect to the reverse stock split, will be available for sale in the public market beginning 180 days after the closing of the Merger as a result of the expiration of lock-up or similar agreements between certain Miragen stockholders and Miragen. All other outstanding shares of common stock will be freely tradable, without restriction, in the public market. In addition, shares of common stock that are subject to outstanding options of Miragen will become eligible for sale in the public market to the extent permitted by the provisions of various vesting agreements and Rules 144 and 701 under the Securities Act. If these shares are sold, the trading price of the combined company s common stock could decline.

If the ownership of the combined company common stock is highly concentrated, it may prevent you and other stockholders from influencing significant corporate decisions and may result in conflicts of interest that could cause the combined company stock price to decline.

Executive officers and directors of the combined company and their affiliates are expected to beneficially own or control approximately 39% of the outstanding shares of common stock of the combined company following the completion of the Merger and assuming that Miragen closes its concurrent financing immediately prior to the effective time of the Merger. Accordingly, these executive officers, directors and their affiliates, acting as a group, will have substantial 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 the combined company assets or any other significant corporate transactions. These stockholders may also delay or prevent a change of control of the combined company, even if such a change of control would benefit the other stockholders of the combined company. The significant concentration of stock ownership may adversely affect the trading price of the combined company s common stock due to investors perception that conflicts of interest may exist or arise.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about the combined company, its business or its market, its stock price and trading volume could decline.

The trading market for the combined company s common stock will be influenced by the research and reports that equity research analysts publish about it and its business. Equity research analysts may elect not to provide research coverage of the combined company s common stock after the completion of this offering, and such lack of research coverage may adversely affect the market price of its common stock. In the event it does have equity research analyst coverage, the combined company will not have any control over the analysts or the content and opinions included in their reports. The price of the combined company s common stock could decline if one or more equity research analysts downgrade its stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of the combined company or fails to publish reports on it regularly, demand for its common stock could decrease, which in turn could cause its stock price or trading volume to decline.

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The combined company will have broad discretion in the use of proceeds from the concurrent financing in connection with the Merger and may invest or spend the proceeds in ways with which you do not agree and in ways that may not increase the value of your investment.

The combined company will have broad discretion over the use of proceeds from Miragen s concurrent financing in connection with the Merger. You may not agree with the combined company s decisions, and its use of the proceeds may not yield any return on your investment. The combined company s failure to apply the net proceeds of the concurrent financing effectively could compromise its ability to pursue its growth strategy and the combined company might not be able to yield a significant return, if any, on its investment of these net proceeds. You will not have the opportunity to influence its decisions on how to use the net proceeds from the concurrent financing.

Because the Merger will result in an ownership change under Section 382 of the Code for Signal, Signal s pre-Merger net operating loss carryforwards and certain other tax attributes will be subject to limitation or elimination. The net operating loss carryforwards and certain other tax attributes of Miragen and of the combined company may also be subject to limitations as a result of ownership changes.

If a corporation undergoes an ownership change within the meaning of Section 382 of the Code, or Section 382, the corporation s net operating loss carryforwards and certain other tax attributes arising from before the ownership change are subject to limitations on use after the ownership change. In general, an ownership change occurs if there is a cumulative change in the corporation s equity ownership by certain stockholders that exceeds fifty percentage points by value over a rolling three-year period. Similar rules may apply under state tax laws. The Merger will result in an ownership change for Signal and, accordingly, Signal s net operating loss carryforwards and certain other tax attributes will be subject to limitation and possibly elimination after the Merger. Miragen has performed an analysis on whether it has experienced any ownership changes in the past. However, it is possible that Miragen s net operating loss carryforwards and certain other tax attributes may also be subject to limitation as a result of prior shifts in equity ownership and/or the Merger. Additional ownership changes in the future could result in additional limitations on Signal s, Miragen s and the combined company s net operating loss carryforwards and certain other tax attributes. Consequently, even if the combined company achieves profitability, it may not be able to utilize a material portion of Signal s, Miragen s or the combined company s net operating loss carryforwards and certain other tax attributes, which could have a material adverse effect on cash flow and results of operations.

If the combined company fails to maintain proper and effective internal controls, its ability to produce accurate financial statements on a timely basis could be impaired.

The combined company will be subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act and the rules and regulations of The NASDAQ Stock Market LLC. The Sarbanes-Oxley Act requires, among other things, that the combined company maintain effective disclosure controls and procedures and internal control over financial reporting. The combined company must perform system and process evaluation and testing of its internal control over financial reporting to allow management to report on the effectiveness of its internal controls over financial reporting in its Annual Report on Form 10-K filing for that year, as required by Section 404 of the Sarbanes-Oxley Act. As a private company, Miragen, has never been required to test its internal controls within a specified period. This will require that the combined company incur substantial professional fees and internal costs to expand its accounting and finance functions and that it expend significant management efforts. The combined company may experience difficulty in meeting these reporting requirements in a timely manner.

The combined company may discover weaknesses in its system of internal financial and accounting controls and procedures that could result in a material misstatement of its financial statements. The combined company s internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how

well designed and operated, can provide only reasonable, not absolute, assurance that the control

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system s objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If the combined company is not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act, or if it is unable to maintain proper and effective internal controls, the combined company may not be able to produce timely and accurate financial statements. If that were to happen, the market price of its common stock could decline and it could be subject to sanctions or investigations by The Nasdaq Stock Market LLC, the SEC, or other regulatory authorities.

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CAUTIONARY STATEMENT CONCERNING FORWARD-LOOKING STATEMENTS

This proxy statement/prospectus/information statement and the documents incorporated by reference into this proxy statement/prospectus/information statement contain forward-looking statements relating to Signal, Miragen and the Merger. These forward-looking statements are based on current expectations and beliefs and involve numerous risks and uncertainties that could cause actual results to differ materially from expectations. These forward-looking statements should not be relied upon as predictions of future events as Miragen and Signal cannot assure you that the events or circumstances reflected in these statements will be achieved or will occur. You can identify forward-looking statements by the use of forward-looking terminology including believes, expects, may, will, should, seeks, plans, pro forma, estimates, or anticipates or the negative of these words and phrases or other variations of these words and phrases or comparable terminology. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. For example, forward-looking statements include any statements regarding the strategies, prospects, plans, expectations or objectives of management of Signal or Miragen for future operations of the combined company, the progress, scope or duration of the development of product candidates or programs, the benefits that may be derived from product candidates or the commercial or market opportunity in any target indication, the ability of Signal or Miragen to protect their intellectual property rights, the anticipated operations, financial position, revenues, costs or expenses of Signal, Miragen or the combined company, statements regarding future economic conditions or performance, statements of belief and any statement of assumptions underlying any of the foregoing. Forward looking statements may also include any statements regarding the approval and closing of the Merger, including the timing of the Merger, Signal s ability to solicit a sufficient number of proxies to approve the Merger, other conditions to the completion of the Merger and the Exchange Ratio as of the closing of the Merger, the expected benefits of the Merger, the ability of Miragen and Signal to complete the Merger, Miragen s ability to complete the concurrent financing of its common stock in connection with the Merger, Signal s ability to complete the sale of its MyPRS intellectual property assets and any statement of assumptions underlying any of the foregoing.

For a discussion of the factors that may cause Signal, Miragen or the combined company s actual results, performance or achievements to differ materially from any future results, performance or achievements expressed or implied in such forward-looking statements, or for a discussion of risk associated with the ability of Signal and Miragen to complete the Merger and the effect of the Merger on the business of Signal, Miragen and the combined company, see Risk Factors beginning on page 19. Additional factors that could cause actual results to differ materially from those expressed in the forward-looking statements are discussed in reports filed with the SEC by Signal. See *Where You Can Find More Information* beginning on page 303. There can be no assurance that the Merger will be completed, or if it is completed, that it will close within the anticipated time period or that the expected benefits of the Merger will be realized.

If any of these risks or uncertainties materialize or any of these assumptions prove incorrect, the results of Signal, Miragen or the combined company could differ materially from the forward-looking statements. All forward-looking statements in this proxy statement/prospectus/information statement are current only as of the date on which the statements were made. Signal and Miragen do not undertake any obligation (and expressly disclaim any such obligation to) to publicly update any forward-looking statement to reflect events or circumstances after the date on which any statement is made or to reflect the occurrence of unanticipated events.

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THE SPECIAL MEETING OF SIGNAL STOCKHOLDERS

Date, Time and Place

The Signal special meeting will be held on February 10, 2017, at 12255 El Camino Real, Suite 300, San Diego, California, 92130, commencing at 9:00 a.m. local time. Signal is sending this proxy statement/prospectus/information statement to its stockholders in connection with the solicitation of proxies by Signal s board of directors for use at the Signal special meeting and any adjournments or postponements of the Signal special meeting. This proxy statement/prospectus/information statement is first being furnished to stockholders of Signal on or about January 17, 2017.

Purposes of the Signal Special Meeting

The purposes of the Signal special meeting are:

1. To approve the issuance of shares of Signal common stock to Miragen stockholders pursuant to the terms of the Merger Agreement, a copy of which is attached as *Annex A*;

2. To approve the change in control of Signal resulting from the Merger contemplated by the Merger Agreement;

3. To approve the conversion of the Note into shares of Signal common stock;

4. To approve the Signal 2016 Equity Incentive Plan, a copy of which is attached as *Annex B*;

5. To approve the Signal 2016 Employee Stock Purchase Plan, a copy of which is attached as *Annex C*;

6. To approve an amendment to the certificate of incorporation of Signal changing the Signal corporate name to Miragen Therapeutics, Inc. in the form attached as *Annex D*;

7. To approve an amendment to the certificate of incorporation of Signal effecting a reverse stock split of Signal s issued and outstanding common stock within a range of every one to 15 shares (or any number in between) of outstanding Signal common stock being combined and reclassified into one share of Signal common stock in the form attached as *Annex E*, which is referred to as the reverse stock split;

8. To approve an amendment to the certificate of incorporation of Signal increasing the number of authorized shares of Signal common stock from 50,000,000 shares to 100,000,000 shares in the form attached as *Annex F*;

9. To approve the sale of all of Signal s intellectual property assets related to its MyPRS test, pursuant to an intellectual property purchase agreement, a copy of which is attached as *Annex G*;

10. To approve an amendment to the certificate of incorporation of Signal to eliminate the ability of Signal stockholders to act by written consent in the form attached as *Annex H*;

11. To consider and vote upon an adjournment of the Signal special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of the proposals set forth above; and

12. To transact such other business as may properly come before the stockholders at the Signal special meeting or any adjournment or postponement thereof.

Each of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9 are conditioned upon each other and the approval of each such proposal is a condition to the completion of the Merger. Therefore, the Merger cannot be consummated without the approval of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9.

Recommendation of Signal s Board of Directors

Signal s board of directors has determined and believes that the issuance of shares of Signal common stock pursuant to the Merger Agreement and the resulting change of control is fair to, in the best

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interests of, and advisable to, Signal and its stockholders and has approved such items. Signal s board of directors recommends that Signal stockholders vote **FOR** Signal Proposal Nos. 1 and 2 to approve the issuance of shares of Signal common stock pursuant to the Merger Agreement and the change of control of Signal resulting from the Merger.

Signal s board of directors has determined and believes that the conversion of the Note into shares of Signal common stock is fair to, in the best interests of, and advisable to, Signal and its stockholders and has approved such item. Signal s board of directors recommends that Signal stockholders vote **FOR** Signal Proposal No. 3 to approve the conversion of the Note.

Signal s board of directors has determined and believes that the approval of the Signal 2016 Equity Incentive Plan and the Signal 2016 Employee Stock Purchase Plan and the reservation of shares of common stock for issuance thereunder is fair to, in the best interests of, and advisable to, Signal and its stockholders and has approved and adopted the plans. Signal s board of directors recommends that Signal stockholders vote **FOR** Proposal Nos. 4 and 5 and the reservation of shares of common stock for issuance thereunder.

Signal s board of directors has determined and believes that the amendment to the certificate of incorporation of Signal to change the name of Signal to Miragen Therapeutics, Inc. is advisable to, and in the best interests of, Signal and its stockholders and has approved such name change. Signal s board of directors recommends that Signal stockholders vote **FOR** Signal Proposal No. 6 to approve the name change.

Signal s board of directors has determined and believes that it is advisable to, and in the best interests of, Signal and its stockholders to approve the amendment to the certificate of incorporation of Signal effecting the reverse stock split, as described in this proxy statement/prospectus/information statement. Signal s board of directors recommends that Signal stockholders vote **FOR** Signal Proposal No. 7 to approve the reverse stock split.

Signal s board of directors has determined and believes that it is advisable to, and in the best interests of, Signal and its stockholders to approve an amendment to the certificate of incorporation of Signal to increase the number of authorized shares of Signal common stock from 50,000,000 shares to 100,000,000 shares. Signal s board of directors recommends that Signal stockholders vote **FOR** Signal Proposal No. 8 to approve the increase in the authorized number of shares of Signal common stock.

Signal s board of directors has determined and believes that the sale of all of Signal s intellectual property assets related to its MyPRS test in the best interests of, and advisable to, Signal and its stockholders and has approved such item. Signal s board of directors recommends that Signal stockholders vote **FOR** Signal Proposal No. 9 to approve the sale of all of Signal s intellectual property assets related to its MyPRS test to Quest Diagnostics Investments LLC.

Signal s board of directors has determined and believes that it is advisable to, and in the best interests of, Signal and its stockholders to approve an amendment to the certificate of incorporation of Signal to eliminate the ability of Signal stockholders to act by written consent. Signal s board of directors recommends that Signal stockholders vote **FOR** Signal Proposal No. 10 to approve the amendment to eliminate the ability of Signal stockholders to act by written consent.

Signal s board of directors has determined and believes that adjourning the Signal special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 is fair to, in the best interests of, and advisable to, Signal and its stockholders and has approved and adopted the proposal. Signal s board of directors recommends that Signal stockholders vote **FOR** Signal Proposal No. 11 to adjourn the Signal special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10.

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Record Date and Voting Power

Only holders of record of Signal common stock at the close of business on the record date, January 9, 2017, are entitled to notice of, and to vote at, the Signal special meeting. At the close of business on the record date, there were 22 holders of record of Signal common stock and there were 742,293 shares of Signal common stock issued and outstanding. Each share of Signal common stock entitles the holder thereof to one vote on each matter submitted for stockholder approval. See the section titled *Principal Stockholders of Signal* beginning on page 297 of this proxy statement/prospectus/information statement for information regarding persons known to the management of Signal to be the beneficial owners of more than 5% of the outstanding shares of Signal common stock.

Voting and Revocation of Proxies

The proxy accompanying this proxy statement/prospectus/information statement is solicited on behalf of Signal s board of directors for use at the Signal special meeting.

If you are a stockholder of record of Signal as of the record date referred to above, you may vote in person at the Signal special meeting or vote by proxy using the enclosed proxy card. Whether or not you plan to attend the Signal special meeting, Signal urges you to vote by proxy to ensure your vote is counted. You may still attend the Signal special meeting and vote in person if you have already voted by proxy. As a stockholder of record:

- to vote in person, attend the Signal special meeting and Signal will give you a ballot when you arrive at the meeting;
- to vote using the proxy card, simply mark, sign and date your proxy card and return it promptly, but in any event, before the Signal special meeting to ensure your shares are voted; or
- to vote by telephone or on the Internet, dial the number on the proxy card or go to the website on the proxy card or voting instruction form to complete an electronic proxy card. You will be asked to provide the company number and control number from the enclosed proxy card. Your vote must be received by February 9, 2017, 11:59 p.m. Eastern Time to be counted.

If your Signal shares are held by your broker as your nominee, that is, in street name, you should receive voting instructions from the bank, broker or other nominee that holds your shares. If you do not give instructions to your broker, your broker can vote your Signal shares with respect to discretionary items but not with respect to non-discretionary items. Discretionary items are proposals considered routine under the rules of The NASDAQ Capital Market on which your broker may vote shares held in street name in the absence of your voting instructions. On non-discretionary items for which you do not give your broker instructions, the Signal shares will be treated as broker non-votes. It is anticipated that Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 will be non-discretionary items. If your shares of Signal common stock are held in street name, you may vote in one the following ways:

- to vote by mail, you should follow the instructions included on the proxy card regarding how to instruct your broker to vote your Signal shares;

to vote in person at the Signal special meeting, you will need to contact the bank, broker or other nominee that is the stockholder of record for your shares to obtain a legal proxy and then bring the legal proxy indicating that you beneficially owned the shares as of the record date and a form of government issued picture identification to the Signal special meeting. If you bring all of these materials to the Signal special meeting, you may vote by completing a paper proxy card or a ballot, which will be available at the Signal special meeting. If you do not bring all of these materials, you will not be able to vote at the Signal special meeting; or

to vote by telephone or over the Internet if you are permitted and wish to do so, you should receive instructions from your bank, broker or other nominee and follow those instructions.

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All properly executed proxies that are not revoked will be voted at the Signal special meeting and at any adjournments or postponements of the Signal special meeting in accordance with the instructions contained in the proxy. If a holder of Signal common stock executes and returns a proxy and does not specify otherwise, the shares represented by that proxy will be voted FOR Signal Proposal No. 1 to approve the issuance of shares of Signal common stock in the Merger, FOR Signal Proposal No. 2 to approve the change of control resulting from the Merger, FOR Signal Proposal No. 3 to approve the conversion of the Note into shares of Signal common stock, FOR Signal Proposal No. 4 to approve the Signal 2016 Equity Incentive Plan, FOR Signal Proposal No. 5 to approve the Signal 2016 Employee Stock Purchase Plan, FOR Signal Proposal No. 6 to approve an amendment to the certificate of incorporation of Signal changing the Signal corporate name to Miragen Therapeutics, Inc., FOR Signal Proposal No. 7 to approve an amendment to the certificate of incorporation of Signal effecting the reverse stock split, FOR Signal Proposal No. 8 to approve the amendment to the certificate of incorporation of Signal to increase the number of authorized shares of Signal common stock, FOR Signal Proposal No. 9 to approve the sale of all of Signal s intellectual property assets related to its MyPRS Test to Quest Diagnostics Investments LLC, FOR Signal Proposal No. 10 to approve an amendment to the certificate of incorporation of Signal to eliminate the ability of Signal stockholders to act by written consent and FOR Signal Proposal No. 11 to adjourn the Signal special meeting, if necessary, to solicit additional proxies if there are not sufficient votes in favor of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 in accordance with the recommendation of Signal s board of directors.

If you are a stockholder of record of Signal and you have not executed a support agreement, you may change your vote at any time before your proxy is voted at the Signal special meeting in any one of the following ways:

- you can send a written notice to the Secretary of Signal before the Signal special meeting stating that you would like to revoke your proxy;
- if you have signed and returned a paper proxy card, you may sign a new proxy card bearing a later date and submit it as instructed above;
- if you have voted by telephone or Internet, you may cast a new vote by telephone or over the Internet as instructed above; or
- you can attend the Signal special meeting and vote in person, but attendance alone will not revoke a proxy. You must specifically request at the meeting that it be revoked.

Required Vote

The presence, in person or represented by proxy, at the Signal special meeting of the holders of a majority of the shares of Signal common stock outstanding and entitled to vote at the Signal special meeting is necessary to constitute a quorum at the meeting. Abstentions and broker non-votes will be counted towards a quorum. The affirmative vote of the holders of a majority of the shares of Signal common stock having voting power present in person or represented by proxy at the Signal special meeting, assuming a quorum is present, is required for approval of Signal Proposal Nos. 1, 2, 3, 4, 5 and 11. The affirmative vote of the holders of a majority of shares of Signal common stock entitled to vote outstanding on the record date for the Signal special meeting is required for approval of Signal Proposal Nos. 6, 7, 8, 9 and 10. Each of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9 are conditioned upon each other and the approval of each such proposal is a condition to the completion of the Merger. Therefore, the Merger cannot be consummated

without the approval of Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9.

Votes will be counted by the inspector of election appointed for the meeting, who will separately count FOR and AGAINST votes, abstentions and broker non-votes. Abstentions will be counted towards the vote total for each proposal and will have the same effect as AGAINST votes for Signal Proposal Nos. 6, 7, 8, 9 and 10, but will have no effect on Signal Proposal Nos. 1, 2, 3, 4, 5 and 11. Similarly, broker non-votes will have the same effect as AGAINST votes for Signal Proposal Nos. 6, 7, 8, 9 and 10, but will have no effect on Signal Proposal Nos. 1, 2, 3, 4, 5 and 11.

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As of December 31, 2016, the directors and executive officers of Signal owned or controlled 26% of the outstanding shares of Signal common stock entitled to vote at the Signal special meeting. The directors and executive officers of Signal owning these shares are subject to support agreements. Each stockholder that entered into a support agreement has agreed to vote all shares of Signal common stock owned by him as of the record date in favor of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 and against any acquisition proposal, as defined in the Merger Agreement.

Solicitation of Proxies

In addition to solicitation by mail, the directors, officers, employees and agents of Signal may solicit proxies from Signal stockholders by personal interview, telephone, telegram or otherwise. Signal and Miragen will share equally the costs of printing and filing this proxy statement/prospectus/information statement and proxy card. Arrangements will also be made with brokerage firms and other custodians, nominees and fiduciaries who are record holders of Signal common stock for the forwarding of solicitation materials to the beneficial owners of Signal common stock. Signal will reimburse these brokers, custodians, nominees and fiduciaries for the reasonable out-of-pocket expenses they incur in connection with the forwarding of solicitation materials. Signal has retained Advantage Proxy to assist it in soliciting proxies using the means referred to above. Signal will pay the fees of Advantage Proxy, which Signal expects to be approximately $7,500, plus reimbursement of out-of-pocket expenses.

Other Matters

As of the date of this proxy statement/prospectus/information statement, Signal s board of directors does not know of any business to be presented at the Signal special meeting other than as set forth in the notice accompanying this proxy statement/prospectus/information statement. If any other matters should properly come before the Signal special meeting, it is intended that the shares represented by proxies will be voted with respect to such matters in accordance with the judgment of the persons voting the proxies.

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THE MERGER

This section and the section titled The Merger Agreement in this proxy statement/prospectus/information statement describe the material aspects of the Merger, including the Merger Agreement. While Signal and Miragen believe that this description covers the material terms of the Merger and the Merger Agreement, it may not contain all of the information that is important to you. You should read carefully this entire proxy statement/prospectus/information statement for a more complete understanding of the Merger and the Merger Agreement, including the Merger Agreement, and the other documents to which you are referred herein. See the section titled Where You Can Find More Information in this proxy statement/prospectus/information statement beginning on page 303.

Background of the Merger

Historical Background of Signal

Signal is currently marketing and selling its MyPRS test to physicians treating patients suffering from multiple myeloma in academic institutions in all 50 states. Signal has been operating at a net loss since inception, based upon a business plan that anticipated raising additional funds through debt or equity financing to operate beyond the second quarter of 2017. Due to current market conditions, Signal s current liquidity position and its depressed stock price, Signal came to believe it would be difficult to obtain additional equity or debt financing on acceptable terms, if at all. As a result, Signal s board of directors began discussing and evaluating its strategic opportunities to maximize stockholder value beginning near the end of 2015. Signal s management provided Signal s board of directors with management s preliminary assessment of a variety of strategic alternatives that Signal could pursue to maximize stockholder value, including engaging in a sale of the company or a merger transaction.

On March 24, 2016, Signal s board of directors decided to move forward to hire an investment bank to serve as financial advisor to the company in exploring and assessing strategic opportunities. Two investment banks were selected for interview based on the qualifications, expertise and reputation of each investment bank and Signal management s and the board s familiarity with their handling of strategic transactions of similar nature (including industry and valuation).

On April 5, 2016, Signal s board of directors and members of Signal s management reviewed proposals from the two investment banks by teleconferences with representatives from each investment bank and ultimately selected Cantor as its financial advisor to advise Signal.

On April 28, 2016, Signal executed an engagement letter with Cantor for Cantor to act as Signal s exclusive financial advisor in connection with, among other things, the possible sale or merger of Signal with a potential acquiror, as well as its exclusive financial advisor and placement agent in connection with a potential capital raise for equity or debt capital.

Beginning in April 2016 and continuing through October 2016, Signal conducted a process of identifying and evaluating potential parties to strategic combinations. In its review of potential public-company combination partners, Signal focused on diagnostic companies possessing the financial resources to integrate MyPRS into their commercial organizations and expand its use among physicians treating patients suffering with multiple myeloma throughout the United States. In its review of potential private company combination partners, Signal focused on biotechnology and diagnostic companies possessing (i) a portfolio of commercialized products or a portfolio of product development candidates with the potential for significant value appreciation, (ii) resources sufficient to achieve potentially meaningful development milestones within such portfolio, including resources to be obtained through financing activities consummated prior to the effectiveness of a combination with Signal, (iii) an ability to enter into an

agreement in the near-term for a combination with a public company (i.e., Signal) and thereafter proceed in an orderly manner toward implementing the combination (necessitating, for example,

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the availability of the requisite financial statements to accompany a registration statement on Form S-4) and (iv) a management team with the breadth and skills to accomplish the foregoing. At the direction of Signal, Cantor contacted over 30 potential parties to gauge their interest in a potential transaction with Signal. On behalf of Signal, Cantor received 12 fully-executed non-disclosure agreements during May and June 2016. In evaluating the indications of interest received in response to this outreach, including in certain cases through discussions and diligence activities with potential counterparties (see in this regard the discussion below with respect to Signal s engagement with Parties 1, 2, 3, 5, 6, 7, 8 and 9), Signal ultimately concluded in each instance that (x) one or more desired elements were missing from a potential combination except with respect to Miragen (for example, that the counterparty did not have sufficient resources to achieve potentially meaningful development milestones within its portfolio of product development candidates, or the counterparty s requirement for Signal to have an unreasonably large cash balance at closing, or the counterparty s uncertain ability to enter into an agreement in the near-term for a combination with a public company), (y) the terms expected to be available to Signal and its stockholders in a potential combination with parties other than Miragen, including as represented by the potential share of the combined company that might be owned by the pre-combination Signal stockholders immediately following a combination and any concurrent financing, would likely not be fair or appropriate to the pre-combination Signal stockholders, and/or (z) Signal should pursue a combination with Miragen and a sale of the assets relating to the MyPRS business to the exclusion of other possibilities. In the course of its process, Miragen is the only party with which Signal ultimately reached a mutual understanding on deal terms, including the potential share of the combined company that would be owned by the pre-combination Signal stockholders immediately following a combination and any concurrent financing, and moved forward with negotiating a definitive merger agreement. A more detailed chronological description of the Merger process follows below under *The Merger Background of the Merger History of Signal Strategic Alternatives and Significant Corporate Events*.

Historical Background of Miragen

Miragen is a clinical stage biopharmaceutical company 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 and play a vital role in influencing the pathways responsible for many disease processes. Miragen believes its experience in bioinformatics, microRNA biology, drug discovery, 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. Miragen uses its expertise in systems biology and oligonucleotide chemistry to develop a pipeline of product candidates.

Miragen s board of directors and executive management regularly review Miragen s operating and strategic plans, both near term and long- term, as well as potential partnerships in an effort to enhance stockholder value, including debt and/or equity financing, mergers and acquisitions, and other strategic transactions, and engaged in discussions with numerous potential strategic partners, lenders and investors, including then current investors in Miragen and potential new investors.

In 2015, the Miragen management team and board began considering an initial public offering of its common stock as well as various other fundraising strategies to fund future research and development activities. During this time, Miragen was approached by a number of investment banks suggesting a reverse merger as an attractive alternative to an initial public offering and the Miragen management team began to consider various reverse merger opportunities as they presented themselves in parallel with exploring an initial public offering.

In May 2016, Miragen management was contacted by a representative of Cantor acting at the direction of and on behalf of Signal regarding Miragen s potential interest in a potential transaction involving Signal, which led to discussions among Miragen s management and several members of Miragen s board of directors and an eventual

indication of interest from Miragen.

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History of Signal Strategic Alternatives and Significant Corporate Events

During May and June, 2016, a confidential information memorandum was circulated, at the direction of Signal, by Cantor to the 12 parties that executed non-disclosure agreements with Signal and expressed interest in pursuing a potential strategic combination with Signal. Following receipt of the confidential information memorandum, one party communicated to Signal that it was not interested in a potential transaction with Signal.

Between May 20, 2016 and June 9, 2016, Signal s management held initial calls with four interested parties, at their request, regarding a potential business combination.

Between June 3, 2016 and June 17, 2016, at the direction of Signal, Cantor distributed process letters to 11 parties asking for bids by June 17, 2016.

Between June 16, 2016 and June 21, 2016, Signal received initial indications of interest from six parties, including Miragen.

On June 21, 2016, Signal s board of directors held a teleconference to review the initial indications of interest and selected four companies to move into the due diligence phase: Party 1, Party 2, Party 3 and Miragen.

On June 24, 2016, at the direction of Signal, Cantor sent second round process letters to the four companies, which indicated that final bids were due by July 29, 2016.

On June 27, 2016, Signal granted access to its virtual data room to personnel representing the four companies for the purposes of reviewing due diligence materials. Party 3 did not respond after obtaining access.

On July 12, 2016, a vice president and two board members representing Party 1 met with Signal s management team (i.e., Samuel D. Riccitelli, president and chief executive officer, Tamara A. Seymour, chief financial officer, and Sudipto Sur, Ph.D., chief information officer) in an extensive diligence meeting. Signal s management team presented information to answer questions submitted by Party 1 prior to the meeting.

On July 15, 2016, Mr. Riccitelli and Ms. Seymour and a representative from Cantor met with Miragen s management team (i.e., William S. Marshall, Ph.D., president and chief executive officer, Jason A. Leverone, chief financial officer, Adam S. Levy, chief business officer, and Christopher J. Morl, former chief operating officer), at Miragen s Boulder, Colorado office for an in-depth review of Miragen s clinical development programs.

On July 19, 2016, Party 1 notified Signal that it would not submit a final indication of interest citing lack of a strategic fit between MyPRS and Party 1 s tests currently in development.

On July 21, 2016, Signal s management provided an update via teleconference to Signal s board of directors, indicating that there were two parties interested in a potential merger transaction, Party 2 and Miragen. Signal management noted that if Signal were to move forward in a merger transaction with Miragen, Miragen had indicated it would require the MyPRS business to be divested or wound down prior to the closing of a merger. Also on July 21, 2016, Signal s chairman contacted Party 5 regarding a potential interest in acquiring MyPRS and determined that Party 5 may be interested. Party 5 indicated that it would be in touch to pursue further conversations.

On July 22, 2016, Signal received a revised indication of interest from Miragen offering Signal stockholders 6% of the fully-diluted stock of the combined company, measured prior to any financing contemplated to take place concurrent with the Merger, with Miragen s stockholders being issued the remaining 94%.

On July 25, 2016, Mr. Riccitelli held an initial conversation by phone with Party 5 s chief operating officer regarding the acquisition of the MyPRS business, and Party 5 agreed to execute a non-disclosure agreement.

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On July 26, 2016, Mr. Riccitelli and Ms. Seymour met with Party 2 s chief executive officer, chief commercial officer, director of finance and financial advisors for an extensive diligence meeting. Each company presented the details of its business.

On July 27, 2016, Party 2 submitted a revised indication of interest, which included the requirement for Signal to have a large cash balance at the closing of a proposed business combination transaction, and offering Signal stockholders 5% of the fully-diluted stock of the combined company, with Party 2 s stockholders being issued the remaining 95%.

On July 29, 2016, Signal s board of directors met to review the two revised indications of interest from Party 2 and Miragen. Signal s board of directors determined that Party 2 s requirement for Signal to have a large cash balance at closing, combined with Party 2 s low cash position and significant outstanding debt, among other things, disqualified Party 2 as a viable combination partner for Signal at that time. In contrast, Signal s board of directors noted that Miragen had a strong balance sheet, experienced management team, strong investor base and viable clinical development program. Therefore, Signal s board of directors decided to move forward with discussions with Miragen. Mr. Riccitelli and Ms. Seymour and a representative from Cantor were instructed by Signal s board of directors to reach out to potential acquirers for the lab business or the intellectual property relating to MyPRS, in addition to Party 5, as Miragen had indicated the divestiture of the MyPRS business would be a condition to Miragen closing a merger transaction. Signal s board of directors also discussed the potential business combination process with its legal counsel, Pillsbury Winthrop Shaw Pittman LLP, or Pillsbury.

During the period of July 31, 2016 through October 6, 2016, Mr. Riccitelli and Ms. Seymour met with, either in person or by phone, Parties 5, 6, 7, 8 and 9 multiple times for diligence discussions regarding potential acquisitions of the MyPRS business. All parties were given access to Signal s virtual data room for the purpose of reviewing due diligence materials. During such time, Parties 6, 7, 8 and 9 notified Signal management, directly or by communication to Cantor, that they would not be submitting a proposal to acquire the MyPRS business or any other transaction. The primary reason cited by these parties for not submitting proposals was the additional cash burn required in the near term to continue to offer the MyPRS test commercially.

On July 29, 2016, at the request of Mr. Riccitelli, Richard A. Bender, M.D., Signal s chief medical officer, contacted Charles Strom, M.D. Ph.D., vice president of research and development for Quest Diagnostics, Incorporated, or Quest, via email, to inquire as to whether Quest might be interested in licensing Signal s MyPRS business. As a result of this communication, on August 5, 2016, Mr. Riccitelli and Dr. Bender met with management and medical team personnel from Quest at Quest s Orange County, California facility for an in-depth review of MyPRS.

On August 5, 2016, Signal received a proposed draft term sheet from Miragen with respect to a proposed business combination between the parties. The draft term sheet provided that the pre-combination Miragen securityholders would collectively receive 94% of fully-diluted stock of the combined company, measured prior to any financing contemplated to occur concurrent with the Merger, and Signal securityholders would hold 6% of the fully-diluted stock of the combined company, with Miragen having the option to conduct a financing that would close concurrent with the Merger and be dilutive to both Signal and Miragen stockholders.

On August 11, 2016, Signal s board of directors reviewed a draft term sheet between Miragen and Signal which outlined a potential business combination between the companies and included reference to a concurrent financing that Miragen intended to complete immediately prior to close of a merger transaction, with such concurrent financing to be dilutive to all securityholders. Signal s board of directors instructed Mr. Riccitelli and Ms. Seymour to continue to negotiate with Miragen regarding a potential business combination between the parties.

On August 15, 2016, Signal and Miragen entered into an amended and restated nondisclosure agreement to include a 30-day exclusivity clause and expand the persons and entities affiliated with Miragen allowed to review Signal s confidential information.

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On August 18, 2016, Quest indicated an interest in moving forward with exploring the potential acquisition of MyPRS to Mr. Riccitelli and requested access to Signal s virtual data room to review due diligence materials.

On August 23, 2016, Miragen s legal counsel, Cooley LLP, or Cooley, sent a draft Merger Agreement to Pillsbury for review on behalf of Signal. The draft Merger Agreement provided that the pre-combination Miragen securityholders would collectively receive 94% of fully-diluted stock of the combined company, measured prior to any financing contemplated to occur concurrent with the Merger, and Signal securityholders would hold 6% of the fully-diluted stock of the combined company. The draft Merger Agreement also provided that Miragen would conduct a financing concurrent with the proposed combination which would be dilutive to all securityholders, and that the two-way termination fee payable by the parties in certain circumstances would be $300,000 plus up to $100,000 in expense reimbursements.

On August 30, 2016, Pillsbury and Cooley held a telephone conference to discuss material issues in the draft Merger Agreement.

On September 6, 2016, Signal s and Miragen s management teams held an all-hands teleconference, in which their respective attorneys and representatives of Cantor also participated, to discuss status of the draft Merger Agreement and Miragen s concurrent financing. Miragen indicated it believed it would be able to finalize commitments for its concurrent financing in the near term.

On September 7, 2016, Cooley sent a revised draft Merger Agreement to Pillsbury.

On September 12, 2016, Pillsbury and Cooley held a telephone conference to discuss material issues in the draft Merger Agreement.

On September 14, 2016, Mr. Riccitelli was informed that Quest s business development committee had approved moving forward with the MyPRS acquisition.

On September 16, 2016, Pillsbury sent a revised draft Merger Agreement to Cooley.

On September 20, 2016, Pillsbury and Cooley held a telephone conference to discuss material issues in the draft Merger Agreement.

On September 26, 2016, Cooley sent a revised draft Merger Agreement to Pillsbury. The draft Merger Agreement provided that the pre-combination Miragen securityholders would collectively receive 94% of fully-diluted capital stock of the combined company, measured prior to any financing concurrent with the Merger, and Signal securityholders would hold 6% of the fully-diluted capital stock of the combined company.

On September 30, 2016, Quest submitted an initial non-binding letter of intent, or LOI, to purchase the lab business from Signal, and then submitted a revised LOI on October 10, 2016 to purchase the intellectual property assets related to MyPRS.

On October 3, 2016, Signal s and Miragen s management teams held an all-hands teleconference, in which their respective attorneys and representatives of Cantor also participated, to discuss status of the draft Merger Agreement and Miragen s concurrent financing. Miragen indicated that it believed the financing would be finalized in the coming weeks.

On October 7, 2016, Party 5 submitted a letter of intent to purchase the lab business. The proposal contained in such letter of intent was not considered a viable offer by Signal s management team and chairman of the board as it included, among other matters, post-closing obligations by Signal personnel to continue employment or consulting for Party 5 that could not be fulfilled by Signal.

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On October 10, 2016, Signal returned a revised LOI to Quest, including revisions that would allow Signal to complete on a concurrent basis both the Merger and the sale to Quest of the MyPRS intellectual property.

On October 10, 2016, Signal s and Miragen s management teams held an all-hands teleconference, in which their respective attorneys and representatives of Cantor also participated, to discuss status of the draft Merger Agreement and Miragen s concurrent financing.

On October 11, 2016, Signal s board of directors reviewed the proposed non-binding Quest LOI to sell the intellectual property assets related to MyPRS and instructed management to negotiate an asset purchase agreement with Quest, subject to the board s further review of such agreement. In addition, Signal s board of directors reviewed Signal s liquidity and cash requirements necessary to meet its obligations, including costs to wind down operations and terminate its employees prior to the closing of the Merger, with and without the sale to Quest of the MyPRS intellectual property.

On October 11, 2016, Mr. Riccitelli and Ms. Seymour, a representative of Pillsbury, and Quest s legal and business development representatives held a teleconference to discuss suggested revisions to the letter of intent. Quest s representatives agreed to seek internal approval on a LOI and return it to Signal as soon as possible.

On October 14, 2016, Signal s and Miragen s management teams held an all-hands teleconference, in which their respective attorneys and representatives of Cantor also participated, to discuss status of the draft Merger Agreement and Miragen s concurrent financing.

On October 18, 2016, Signal s and Miragen s management teams held an all-hands teleconference, in which their respective attorneys and representatives of Cantor also participated, to discuss status of the draft Merger Agreement and Miragen s concurrent financing.

On October 18, 2016, Signal received the revised draft Quest LOI in substantially the same form as presented by Signal to Quest per the draft of October 10, 2016.

On October 19, 2016, Mr. Riccitelli and Mr. Marshall, the chief executive officers of Signal and Miragen, respectively, discussed Miragen s concurrent financing via telephone. Mr. Marshall expressed confidence in a near-term commitment for the proposed concurrent financing.

On October 19, 2016, Signal s board of directors reaffirmed its instruction to management to negotiate an asset purchase agreement with Quest based on the Quest LOI dated October 18, 2016, subject to the board s further review of such agreement.

On October 24, 2016, Signal s and Miragen s management teams held an all-hands teleconference, in which their respective attorneys and representatives of Cantor also participated, to discuss status of the draft Merger Agreement and Miragen s concurrent financing. Miragen s management indicated that a commitment for the financing had been secured and terms were agreed. They also indicated that they expected to receive subscription agreements for approximately $40 million and to have the executed subscription agreements within the coming week.

On October 26, 2016, Signal s and Miragen s management teams held an all-hands teleconference, in which their respective attorneys and representatives of Cantor also participated, to discuss status of the draft Merger Agreement and Miragen s concurrent financing. Miragen confirmed that the financing would total approximately $40 million. The parties agreed that the Merger Agreement would be finalized by October 31, 2016, if possible. Signal and Miragen each agreed that they would schedule board meetings for October 31, 2016 to consider the proposed Merger

Agreement. In addition, Signal s projected net cash position of less than zero at Merger closing was discussed. It was agreed that Signal and Miragen s chief executive officers would speak separately to resolve the issue.

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On October 27, 2016, Messrs. Riccitelli and Marshall discussed the potential for Signal s net cash position to be less than zero at closing of the Merger due to delays in the transaction. In the course of those discussions, mutually acceptable thresholds and formulas with respect to net cash were developed to be included in the proposed Merger Agreement.

On October 27, 2016, Mr. Riccitelli and Ms. Seymour and Pillsbury held a teleconference with Quest s general manager of oncology, legal counsel and business development representative to discuss the diligence process. The parties agreed to a target date for executing a definitive purchase agreement for Signal s intellectual property assets for its MyPRS test, presuming the completion of satisfactory due diligence.

Between October 27, 2016 and November 23, 2016, there were various teleconferences, in-person meetings, facility tours and email communications among Mr. Riccitelli, Ms. Seymour and Dr. Sur and representatives from Quest s business development, informatics, operations and management teams regarding Quest s due diligence review of Signal s MyPRS test.

On October 28, 2016, Signal and Miragen agreed to Signal s net cash definition and thresholds to be included in the proposed Merger Agreement and the draft was finalized.

On October 29, 2016, Mr. Riccitelli distributed to Signal s board of directors copies of the proposed Merger Agreement with respect to a proposed business combination transaction between Signal and Miragen, proposed resolutions for adoption by Signal s board of directors if it elected to authorize Signal s management to proceed with such transaction, and related transaction documents, for review prior to the board meeting scheduled for October 31, 2016.

On October 29, 2016, Cooley distributed to Miragen s board of directors copies of the proposed Merger Agreement and Subscription Agreement, proposed resolutions for adoption by Miragen s board of directors if it elected to authorize Miragen s management to proceed with such transactions, and related transaction documents for review prior to the board meeting scheduled for October 31, 2016.

On October 31, 2016, Signal s board of directors held a meeting that representatives of Pillsbury and Cantor attended at the invitation of Signal s board of directors. During the meeting, members of Signal s management reviewed the key features of the proposed business combination between Signal and Miragen, including: structure and timing considerations; the Exchange Ratio for the conversion of Miragen capital stock into Signal common stock as well as the relative percentages of ownership of the existing Signal stockholders, on the one hand, and the Miragen stockholders (including investors in Miragen s planned concurrent financing), on the other hand, following the completion of the Merger; the planned concurrent financing of Miragen; the terms of support agreements from certain Miragen directors, officers, stockholders and affiliates, as well as Signal directors, officers and affiliates, to vote in favor of the proposed business combination; the closing conditions in the Merger Agreement as well as the subscription agreement for Miragen s planned concurrent financing; and the termination provisions and termination fees set forth in the Merger Agreement. In addition, representatives of Cantor reviewed with Signal s board of directors Cantor s analysis of the Exchange Ratio for the conversion of Miragen capital stock into Signal common stock and rendered Cantor s opinion to Signal s board of directors (in its capacity as such), subsequently confirmed by delivery of a written opinion on that same day, that, as of October 31, 2016 and based upon and subject to the assumptions made, procedures followed, matters considered, and qualifications and limitations set forth in the opinion, the Exchange Ratio for the conversion of Miragen capital stock into Signal common stock was fair from a financial point of view to Signal. Representatives from Pillsbury reviewed with Signal s board of directors the fiduciary duties of the board members in the context of the proposed business combination. During the various discussions, Signal s board of directors asked questions and discussed the terms and features of the proposed business combination, including

provisions of the proposed Merger Agreement and related documentation, as well as Signal s cash forecast and ability to satisfy its obligations prior to the projected closing date in light of the net cash requirement contained in the Merger Agreement. After further discussion among Signal s board of directors, the board unanimously (i) determined

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that the Merger and the other transactions contemplated by the Merger Agreement were fair to and in the best interests of Signal and its stockholders, (ii) approved and adopted the Merger Agreement and the transactions contemplated thereby, subject to finalization of the Merger Agreement and ancillary documents by Signal s management in consultation with Signal s legal counsel, with such changes thereto as Signal s management deems to be in the best interests of Signal and its stockholders, (iii) resolved to recommend that the Signal stockholders vote to approve the Merger, adopt the Merger Agreement and approve and/or adopt the other transactions and arrangements as contemplated by the Merger Agreement, including the issuance of shares of Signal common stock in the Merger, (iv) approved the Note Amendment to make the Note convertible into shares of Signal common stock in connection with the Merger and pursuant to the terms of the Note Amendment that had been distributed for review in advance of the meeting, and (v) approved a reverse split of Signal s common stock in a ratio of one-for-15 to be effective at 5:01 p.m. Eastern Time on November 4, 2016, which reverse split had been previously approved by Signal stockholders at the annual meeting.

Later that day, members of the Signal s and Miragen s management teams met, together with representatives of Pillsbury and Cooley, to finalize the Merger Agreement and related transaction documents. After finalization, Signal and Miragen entered into the Merger Agreement and related transaction documents.

Signal Reasons for the Merger

Signal s board of directors considered the following factors in reaching its conclusion to approve and adopt the Merger Agreement and the transactions contemplated thereby and the sale of the MyPRS intellectual property assets and to recommend that the Signal stockholders approve the Merger, adopt the Merger Agreement and other transactions contemplated by the Merger Agreement, including the issuance of shares of Signal common stock in the Merger and approve the sale of the MyPRS intellectual property assets, all of which Signal s board of directors viewed as supporting its decision to approve the business combination with Miragen:

Signal s board of directors believes, based in part on the judgment, advice and analysis of Signal management with respect to the potential strategic, financial and operational benefits of the Merger (which judgment, advice and analysis was informed in part on the business, technical, financial, accounting and legal due diligence investigation performed with respect to Miragen), that:

Miragen is 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;

the combined company will be led by an experienced senior management team from Miragen and a board of directors of seven members designated by Miragen; and

Miragen has commitments for $40.7 million to fund Miragen s development pipeline from an investor syndicate that includes its existing venture investors, Brace Pharma Capital, Atlas Venture, Boulder Ventures, JAFCO Co., Ltd., MP Healthcare Venture Management, MRL Ventures (a venture fund of Merck, known as MSD outside the United States and Canada), Remeditex Ventures, as well as new investors, Fidelity Management and Research Company. Although not a condition to the completion of

the Merger, if closed the concurrent financing, in addition to $16.1 million from the second tranche of Miragen s Series C Preferred Stock funding, which closed prior to execution of the definitive Merger Agreement, is expected to provide sufficient funding to advance Miragen s clinical development programs. Each of Miragen s clinical programs has the potential, if successful, to create value for the stockholders of the merged company and present the combined company with additional fund raising opportunities in the future.

Signal s board of directors also reviewed with the management of Signal the current plans of Miragen for developing its clinical programs to confirm the likelihood that the combined company would possess sufficient financial resources to allow the management team to focus initially on the continued

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development of its clinical programs. Signal s board of directors also considered the possibility that the combined company would be able to take advantage of the potential benefits resulting from the combination of Signal and Miragen to raise additional funds in the future.

Signal s board of directors considered the opportunity as a result of the Merger for Signal stockholders to participate in the potential value that may result from development of the Miragen clinical development programs and the potential increase in value of the combined company following the Merger.

Signal s board of directors concluded that the Merger would provide the existing Signal stockholders with an opportunity to participate in the potential increase in value of the combined company following the Merger.

Signal s board of directors considered the opinion of Cantor delivered to Signal s board of directors (in its capacity as such) that, as of October 31, 2016 and based upon and subject to the assumptions made, procedures followed, matters considered, and qualifications and limitations set forth in the opinion, the Exchange Ratio for the conversion of Miragen capital stock into Signal common stock pursuant to the Merger Agreement, was fair to Signal from a financial point of view, as more fully described below under the section titled *The Merger Opinion of Signal s Financial Advisor.*

Signal s board of directors also reviewed various factors impacting the financial condition, results of operations and prospects for Signal, including:

- the strategic alternatives of Signal to the Merger, including potential transactions that could have resulted from discussions that Signal s management conducted with other potential merger partners;
- the consequences of current market conditions, Signal s current liquidity position, its depressed stock price and continuing net operating losses, and the likelihood that the resulting circumstances for the company would not change for the benefit of the Signal stockholders in the foreseeable future on a stand-alone basis;
- the risks of continuing to operate Signal on a stand-alone basis, including the need to continue building the company s tests services menu, infrastructure and management team to support the laboratory services business with insufficient capital resources; and
- Signal management s belief that it would be difficult to obtain additional equity or debt financing on acceptable terms, if at all.

Signal s board of directors also reviewed the terms and conditions of the proposed Merger Agreement and associated transactions, as well as the safeguards and protective provisions included therein intended to mitigate risks, including:

the Exchange Ratio used to establish the number of shares of Signal common stock to be issued in the Merger, and the expected relative percentage ownership of Signal stockholders and Miragen stockholders immediately following the completion of the Merger;

the planned concurrent financing in Miragen, the limited number and nature of conditions to the obligation of the proposed investors in Miragen to consummate the planned concurrent financing, and the ability of Signal to specifically enforce the obligations of the investors to complete the investment in Miragen if all of such conditions have been satisfied;

the limited number and nature of the conditions to the Miragen obligation to consummate the Merger and the limited risk of non-satisfaction of such conditions as well as the likelihood that the Merger will be consummated on a timely basis;

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the respective rights of, and limitations on, Signal and Miragen under the Merger Agreement to consider certain unsolicited acquisition proposals under certain circumstances should Signal or Miragen receive a superior competing proposal;

the reasonableness of the potential termination fee of $300,000 and/or expense reimbursements of up to $100,000, which could become payable by either Signal or Miragen if the Merger Agreement is terminated in certain circumstances;

the support agreements, pursuant to which certain directors, officers and affiliated stockholders of Miragen agreed, solely in their capacity as stockholders, to vote all of their shares of Miragen capital stock in favor of adoption of the Merger Agreement;

the agreement of Miragen to provide written consent of its stockholders necessary to adopt the Merger Agreement thereby approving the Merger and related transactions within five business days of the registration statement on Form S-4, of which this proxy statement/prospectus/information statement is a part, becoming effective; and

the belief that the terms of the Merger Agreement, including the parties representations, warranties and covenants, and the conditions to their respective obligations, are reasonable under the circumstances.

In the course of its deliberations, Signal s board of directors also considered a variety of risks and other countervailing factors related to entering into the Merger, including:

the $300,000 termination fee and/or expense reimbursements of up to $100,000 that may be payable by Signal to Miragen upon the occurrence of certain events, and the potential effect of such termination fee or reimbursement of transaction expenses in deterring other potential acquirors from proposing a competing transaction that may be more advantageous to Signal stockholders;

the substantial expenses to be incurred in connection with the Merger;

the possible volatility, at least in the short term, of the trading price of the Signal common stock resulting from the Merger announcement;

the risk that the Merger might not be consummated in a timely manner, or at all, and the potential adverse effect of the public announcement of the Merger or on the delay or failure to complete the Merger on the reputation of Signal;

the risk that if the sale of the MyPRS business is not completed, then Signal would have incurred additional expenses that may not allow it to meet the closing net cash requirement of the Merger Agreement;

the risk to Signal s business, operations and financial results in the event that the Merger is not consummated;

the strategic direction of the continuing entity following the completion of the Merger, which will be determined by a board of directors initially designated entirely by Miragen;

the fact that the Merger would give rise to substantial limitations on the utilization of Signal s NOLs;

the ability to amend the Note so that the indebtedness would convert into shares of Signal common stock; and

various other risks associated with the combined company and the Merger, including those described in the section titled *Risk Factors* in this proxy statement/prospectus/information statement.

The foregoing information and factors considered by Signal s board of directors are not intended to be exhaustive, but are believed to include all of the material factors considered by Signal s board of directors. In view of the wide variety of factors considered in connection with its evaluation of the Merger and the complexity

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of these matters, Signal s board of directors did not find it useful to attempt, and did not attempt, to quantify, rank or otherwise assign relative weights to these factors. In considering the factors described above, individual members of Signal s board of directors may have given different weight to different factors. Signal s board of directors conducted an overall analysis of the factors described above, including thorough discussions with, and questioning of, the Signal management team and the legal and financial advisors of Signal, and considered the factors overall to be favorable to, and to support, its determination.

Miragen Reasons for the Merger

In the course of reaching its decision to approve the Merger, Miragen s board of directors consulted with its senior management, financial advisor and legal counsel, reviewed a significant amount of information and considered a number of factors, including, among others:

- the potential to provide its current stockholders with greater liquidity by owning stock in a public company;
- the potential to access of public market capital, including sources of capital from a broader range of investors to support the clinical development of its product candidates than it could otherwise obtain if it continued to operate as a privately-held company;
- the expectation that the Merger would be a more time- and cost-effective means to access capital than other options considered, including an initial public offering which Miragen was alternatively planning to pursue;
- the fact that shares of Signal common stock issued to Signal stockholders will be registered pursuant to a registration statement on Form S-4 by Signal and will become freely tradable for Miragen s stockholders who are not affiliates of Miragen;
- the likelihood that the Merger will be consummated on a timely basis;
- the terms and conditions of the Merger Agreement, including, without limitation, the following:
  - the determination that an exchange ratio that is not subject to adjustment based on trading prices is appropriate to reflect the expected relative percentage ownership of Signal securityholders, Miragen securityholders and securityholders of those shares sold in the concurrent financing was appropriate based, in the judgment of Miragen s board of directors;
  - the expectation that the Merger will be treated as a reorganization for U.S. federal income tax purposes, with the result that the Miragen stockholders will not recognize taxable gain or loss for U.S. federal income tax purposes upon the exchange of Miragen common stock for Signal common stock pursuant to the Merger;

the rights of Miragen under the Merger Agreement to consider certain unsolicited competing proposals under certain circumstances should Miragen receive a superior proposal; and

the conclusion of Miragen s board of directors that the potential termination fee of $300,000 and/or expense reimbursements of up to $100,000, payable by Signal to Miragen and the circumstances when such fee may be payable, were reasonable.

Miragen s board of directors also considered a number of uncertainties and risks in its deliberations concerning the Merger and the other transactions contemplated by the Merger Agreement, including the following:

the possibility that the Merger might not be completed and the potential adverse effect of the public announcement of the Merger on the reputation of Miragen and the ability of Miragen to obtain financing in the future in the event the Merger is not completed;

the termination fee of $300,000 and/or expense reimbursements of up to $100,000, payable by Miragen to Signal upon the occurrence of certain events, and the potential effect of such termination fee in deterring other potential acquirers from proposing a competing transaction that may be more advantageous to Miragen s stockholders;

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the risk that the Merger might not be consummated in a timely manner or at all;

the expenses to be incurred in connection with the Merger and related administrative challenges associated with combining the companies;

the additional public company expenses and obligations that Miragen s business will be subject to following the Merger to which it has not previously been subject; and

various other risks associated with the combined company and the Merger, including the risks described in the section titled *Risk Factors* in this proxy statement/prospectus/information statement.

The foregoing information and factors considered by Miragen s board of directors are not intended to be exhaustive, but are believed to include all of the material factors considered by Miragen s board of directors. In view of the wide variety of factors considered in connection with its evaluation of the Merger and the complexity of these matters, Miragen s board of directors did not find it useful, and did not attempt, to quantify, rank or otherwise assign relative weights to these factors. In considering the factors described above, individual members of Miragen s board of directors may have given different weight to different factors. Miragen s board of directors conducted an overall analysis of the factors described above, including thorough discussions with, and questioning of, Miragen s management and Miragen s legal advisors, and considered the factors overall to be favorable to, and to support, its determination.

Opinion of Signal Financial Advisor

On April 28, 2016, Signal engaged Cantor to act as Signal s financial advisor in connection with potential strategic alternatives for Signal. As part of this engagement, Signal s board of directors requested that Cantor evaluate the fairness, from a financial point of view, to Signal of the Exchange Ratio for the conversion of Miragen common stock into Signal common stock pursuant to the Merger Agreement. On October 31, 2016, at a meeting of Signal s board of directors, Cantor rendered its oral opinion to Signal s board of directors (in its capacity as such), which opinion was subsequently confirmed by delivery of a written opinion dated October 31, 2016, that, as of such date and based upon and subject to the assumptions made, procedures followed, matters considered, and qualifications and limitations set forth in the opinion, the Exchange Ratio for the conversion of Miragen common stock into Signal common stock pursuant to the Merger Agreement was fair, from a financial point of view, to Signal.

The full text of the written opinion of Cantor, dated October 31, 2016, which sets forth, among other things, the assumptions made, procedures followed, matters considered and qualifications and limitations of the review undertaken in connection with such opinion, is attached as *Annex I*. Holders of Signal common stock are urged to read this opinion carefully and in its entirety. Cantor s opinion was provided for the sole benefit and use of Signal s board of directors (in its capacity as such) in connection with its consideration of the Merger and addresses only the fairness to Signal, from a financial point of view, of the Exchange Ratio for the conversion of Miragen common stock into Signal common stock pursuant to the Merger Agreement. It does not address any other aspects of the Merger and does not constitute a recommendation as to how holders of Signal common stock or Miragen common stock should vote or act in connection with the Merger. The Exchange Ratio was determined through negotiations between Signal and Miragen and not pursuant to any recommendation of Cantor. The summary of the opinion below is qualified in its entirety by reference to the full text of the opinion.

In the course of performing its review and analyses for rendering its opinion, Cantor, among other things:

reviewed a draft of the Merger Agreement, dated October 30, 2016;

reviewed a draft of the Subscription Agreement, dated October 30, 2016;

reviewed certain publicly available business and financial information relating to Signal and Miragen;

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reviewed certain operating and financial information relating to Signal and Miragen s respective businesses and Signal s prospects, as provided to Cantor by Signal s and Miragen s management, including projections for Signal for the five years ended December 31, 2020, and monthly cash projections for October, November, and December 2016, as prepared and provided to Cantor by Signal s management;

held conference calls with certain members of Signal s senior management and Signal s board of directors to discuss Signal s and Miragen s respective businesses, operations, historical and projected financial results and future prospects;

held conference calls with certain members of Miragen s senior management to discuss Miragen s business and operations;

reviewed certain publicly available information with respect to other companies in the biopharmaceutical industry that Cantor deemed to be relevant;

reviewed the financial terms, to the extent publicly available, of selected recent business combinations and initial public offerings involving companies in the biopharmaceutical industry that Cantor deemed to be relevant; and

conducted such other studies, analyses, inquiries and investigations as Cantor deemed appropriate.

In rendering its opinion, Cantor relied upon and assumed, without independent verification, the accuracy and completeness of the financial and other information provided to or discussed with it by Signal and Miragen or obtained by it from public sources, including, without limitation, the projections referred to above. With respect to the projections, Cantor relied on representations that they have been reasonably prepared on bases reflecting the best currently available estimates and judgments of the senior management of Signal, as to the expected future performance of and liquidation value of Signal. Cantor assumed no responsibility for the independent verification of any such information, including, without limitation, the projections, and expressed no view or opinion as to such projections and the assumptions upon which they were based. Cantor further relied upon the assurances of senior management of Signal that they were unaware of any facts that would make the information and projections incomplete or misleading. Cantor also relied upon, without independent verifications, the assessment of Signal management and Miragen management as to the viability of, and risks associated with, the current and future products and services of Miragen (including without limitation, the development, testing and marketing of such products and services, the receipt of all necessary governmental and other regulatory approvals for the development, testing and marketing thereof, and the life and enforceability of all relevant patents and other intellectual and other property rights associated with such products and services). Cantor assumed that the executed Merger Agreement and Subscription Agreement would not differ in any material respect from the drafts thereof reviewed by Cantor, and that the Merger and Miragen s concurrent financing would be consummated in accordance with the terms of the Merger Agreement and the Subscription Agreement, respectively, without waiver, modification or amendment and in compliance with all applicable laws, documents and other requirements. Cantor also assumed that in the course of obtaining the necessary regulatory or third-party approvals, consents and releases for the Merger, no delay, limitation, restriction or condition would be imposed that would have an adverse effect on Signal, Miragen, or the contemplated benefits of the Merger. Cantor also assumed that the representations and warranties of the parties to the Merger Agreement contained therein were true and correct in all respects material to Cantor s analysis. Cantor also assumed, at the direction of Signal

management, that the Miragen allocation percentage would be no greater than 0.94.

In arriving at its opinion, Cantor did not perform or obtain any independent evaluation or appraisal of the assets or liabilities (contingent or otherwise) of Signal and Miragen, nor did it conduct a physical inspection of any of the properties or facilities of Signal or Miragen, nor was it furnished with any such evaluations, appraisals or inspections, nor did it assume any responsibility to obtain any such evaluations, appraisals or inspections. During the course of its engagement, Cantor was directed by Signal s board of directors to solicit indications of interest from various third parties regarding a transaction with Signal, and it considered the results of such solicitation in

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rendering its opinion. Cantor is not a legal, tax, regulatory or accounting advisor and relied on the assessments made by Signal and its advisors with respect to such issues. Cantor s opinion does not address any legal, tax, regulatory or accounting matters.

Cantor did not express any opinion as to the range of prices at which the shares of Signal common stock may trade subsequent to the announcement or consummation of the Merger or at any time.

The opinion of Cantor was intended solely for the benefit and use of Signal s board of directors (in its capacity as such) in connection with its consideration of the Merger. Cantor s opinion is not to be used for any other purpose, or to be reproduced, disseminated, quoted from or referred to at any time, in whole or in part, without its prior written consent; provided, however, that Cantor authorized the inclusion of its written opinion in its entirety in this proxy statement/prospectus/information statement. Cantor s opinion does not constitute a recommendation to Signal s board of directors in connection with the Merger, nor does it constitute a recommendation to any holders of Signal common stock or Miragen common stock as to how to vote or act in connection with the Merger. Cantor s opinion addressed only the fairness of the Exchange Ratio for the conversion of Miragen common stock into Signal common stock pursuant to the Merger Agreement from a financial point of view to Signal. Cantor s opinion did not address Signal s underlying business decision to pursue the Merger, the relative merits of the Merger as compared to any alternative business or financial strategies that might exist for Signal or the effects of any other transaction in which Signal might engage. In addition, Cantor s opinion did not constitute a solvency opinion or a fair value opinion, and Cantor did not evaluate the solvency or fair value of Signal under any federal or state laws relating to bankruptcy, insolvency or similar matters. Furthermore, Cantor did not express any view or opinion as to the fairness, financial or otherwise, of the amount or nature of any compensation payable to or to be received by any of Signal s officers, directors or employees, or any class of such persons, in connection with the Merger relative to the Exchange Ratio. Cantor expressed no view as to any other aspect or implication of the Merger or any other agreement, arrangement or understanding entered into in connection with the Merger or otherwise, and expressed no opinion as to the terms of Miragen s concurrent financing or the sale of all of Signal s intellectual property assets related to its MyPRS test.

Cantor s opinion was authorized for issuance by the Fairness Opinion and Valuation Committee of Cantor. Cantor s opinion is subject to the assumptions, limitations, qualifications and other conditions contained therein and is necessarily based on economic, market and other conditions, and the information made available to Cantor, as of the date thereof. Cantor assumed no responsibility for updating or revising its opinion based on circumstances or events of which it becomes aware after the date thereof.

The following is a summary of the material analyses performed by Cantor in preparing its opinion, dated October 31, 2016, to Signal s board of directors (in its capacity as such). The preparation of an opinion necessarily is not susceptible to partial analysis or summary description. In performing its analyses, Cantor did not attribute any particular weight to any analysis, methodology or factor considered by it, but rather made qualitative judgments as to the significance and relevance of each analysis and factor. Accordingly, Cantor s illustrative analyses must be considered as a whole. Considering any portion of the analyses or the factors considered, without considering all analyses and factors, could create a misleading or incomplete view of Cantor s analyses.

Selected IPO Analysis

Oncology IPO Companies. Using publicly available information, Cantor reviewed the implied pre-money equity valuations of seven selected biotechnology companies with a therapeutic focus on oncology that completed an initial public offering between September 2013 and October 2016 which raised a minimum of $40 million. The implied pre-money equity valuation is defined as the equity valuation of a company implied by the offering price of such company s shares in its initial public offering, minus the total gross proceeds of the initial public offering. Cantor noted

that, although such companies were deemed relevant for comparative purposes, they may differ from Miragen in one or more ways, including, but not limited to, indications for technology, size and

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competitive nature of targeted markets, number of compounds, scientific evidence, attractiveness of pre-clinical and clinical data, perceived quality of management, the boards of directors and investors, intellectual property, cash resources or financial position, and partnerships. Accordingly, there are inherent limitations on the applicability of such companies to the illustrative analysis of Miragen. These selected companies, which are referred to as the Oncology IPO Companies, were:

Syros Pharmaceuticals, Inc.

Corvus Pharmaceuticals, Inc.

Mirna Therapeutics, Inc.

Loxo Oncology, Inc.

Immune Design Corp.

MacroGenics, Inc.

Five Prime Therapeutics, Inc.

Cantor observed a range of implied pre-money equity valuations for the selected Oncology IPO Companies of between $97 million and $304 million with a mean and median implied pre-money equity valuation of $184 million and $146 million, respectively. Cantor then compared the implied equity values attributable to the 3.1% of the combined company to be held immediately following the Merger by holders of Signal common stock at the time of Cantor s opinion of approximately $5.7 million and $4.5 million based on the mean and median, respectively, implied pre-money equity valuations for the selected Oncology IPO Companies to Signal s estimated liquidation value, per Signal management, of negative $559,000.

Early Stage IPO Companies. Using publicly available information, Cantor reviewed the implied pre-money equity valuations of six selected biotechnology companies that had a focus outside of oncology, but which were considered early stage because they had no product candidate beyond Phase 1 clinical trials, who completed initial public offerings between September 2013 and October 2016 which raised a minimum of $40 million. Cantor noted that although such companies were deemed relevant for comparative purposes, they may differ from Miragen in one or more ways, including, but not limited to, indications for technology, size and competitive nature of targeted markets, number of compounds, scientific evidence, attractiveness of pre-clinical and clinical data, perceived quality of management, the boards of directors and investors, intellectual property, cash resources or financial position, and partnerships. Accordingly, there are inherent limitations on the applicability of such companies to the illustrative analysis of Miragen. These selected companies, which are referred to as the Early Stage IPO Companies, were:

Ra Pharmaceuticals, Inc.

Protagonist Therapeutics, Inc.

AveXis, Inc.

Voyager Therapeutics, Inc.

MyoKardia, Inc.

Nivalis Therapeutics, Inc.

Cantor observed a range of implied pre-money equity valuations for the selected Early Stage IPO Companies of between $106 million and $353 million, with a mean and median implied pre-money equity valuation of $213 million $198 million, respectively. Cantor then compared the implied equity values attributable to the 3.1% of the combined company to be held immediately following the Merger by holders of Signal common stock at the time of Cantor s opinion of approximately $6.6 million and $6.2 million based on the mean and median, respectively, implied pre-money equity valuations for the selected Early Stage IPO Companies to Signal s estimated liquidation value, per Signal management, of negative $559,000.

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Selected Companies Analysis

Oncology Companies. Using publicly available information, Cantor reviewed selected financial data of six selected publicly-traded companies that had aggregate market capitalizations under $500 million and which had a therapeutic focus on oncology. Cantor noted that, although such companies were deemed relevant for comparative purposes, they may differ from Miragen in one or more ways, including, but not limited to, indications for technology, size and competitive nature of targeted markets, number of compounds, scientific evidence, attractiveness of pre-clinical and clinical data, perceived quality of management, the boards of directors and investors, intellectual property, cash resources or financial position, and partnerships. Accordingly, there are inherent limitations on the applicability of such companies to the illustrative analysis of Miragen. These selected companies, which are referred to as the Oncology Companies, were:

Bellicum Pharmaceuticals, Inc.

CytomX Therapeutics, Inc.

Lion Biotechnologies, Inc.

Curis, Inc.

Adaptimmune Therapeutics plc

Idera Pharmaceuticals, Inc.

Cantor observed a range of implied equity valuations for the selected Oncology Companies of between $312 million and $467 million, with a mean and median implied equity valuation of $384 million and $377 million, respectively. Cantor then compared the implied equity values attributable to the 3.1% of the combined company to be held immediately following the Merger by holders of Signal common stock at the time of Cantor s opinion of approximately $12.0 million and $11.7 million based on the mean and median, respectively, implied equity valuations for the selected Oncology Companies to Signal s estimated liquidation value, per Signal management, of negative $559,000.

Early Stage Companies. Using publicly available information, Cantor reviewed selected financial data of three selected publicly-traded companies that had aggregate market capitalizations under $500 million and which were considered early stage because they had no product candidate beyond Phase 1 clinical trials (with the exception of Regulus Therapeutics Inc., which has one program in Phase 2 clinical development with two indications). Cantor noted that, although such companies were deemed relevant for the comparative purposes, they may differ from Miragen in one or more ways, including, but not limited to, indications for technology, size and competitive nature of targeted markets, number of compounds, scientific evidence, attractiveness of pre-clinical and clinical data, perceived quality of management, the boards of directors and investors, intellectual property, cash resources or financial position, and partnerships. Accordingly, there are inherent limitations on the applicability of such companies to the illustrative analysis of Miragen. These selected companies, which are referred to as the Early Stage Companies, were:

Regulus Therapeutics Inc.

ProQR Therapeutics N.V.

ContraFect Corporation

Cantor observed a range of implied equity valuations for selected the Early Stage Companies of between $89 million and $141 million, with a mean and median implied equity valuation of $119 million and $128 million, respectively. Cantor then compared the implied equity values attributable to the 3.1% of the combined company to be held immediately following the Merger by holders of Signal common stock at the time of Cantor s opinion of approximately $3.7 million and $4.0 million based on the mean and median, respectively, implied equity valuations for the selected Early Stage Companies to Signal s estimated liquidation value, per Signal management, of negative $559,000.

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Selected Transactions Analysis

Cantor reviewed publicly available information relating to six selected acquisition transactions, announced since the beginning of 2013, of companies in the biopharmaceutical industry which had either a therapeutic focus on oncology or no products beyond Phase 1 at the time of announcement of the transaction, in each case with an aggregate transaction valuation (based solely upon upfront payments and excluding contingent value rights or other post-closing payments) of less than $1 billion. Cantor noted that, although the companies that were acquired in the selected acquisitions had certain financial and operating characteristics that could be considered similar to those of Miragen, none of these companies had the same management, make-up, technology, size or mix of business as Miragen. Accordingly, there are inherent limitations on the applicability of such companies to the illustrative analysis of Miragen. Additionally, based on publicly available information, none of the target companies in such acquisitions was in the process of winding down operations at the time of the acquisition. Cantor also noted that there have been varying market conditions over the time periods during which the selected acquisitions were announced. These acquisitions, which are referred to as the Selected Transactions, were:

acquisition of Vitae Pharmaceuticals, Inc. by Allergan plc (announced September 14, 2016)

acquisition of Admune Therapeutics LLC by Novartis AG (announced October 21, 2015)

acquisition of OnCore Biopharma, Inc. by Arbutus Biopharma Inc. (fka. Tekmira Pharmaceuticals) (announced January 11, 2015)

acquisition of iPierian, Inc. by Bristol-Myers Squibb Company (announced April 29, 2014)

acquisition of Sirna Therapeutics, Inc. by Alnylam Pharmaceuticals, Inc. (announced January 12, 2014)

acquisition of Amplimmune, Inc. by MedImmune, LLC (announced August 26, 2013)

Cantor observed a range of the disclosed upfront consideration at the time of announcement for the Selected Transactions, not adjusted for stock price differences since announcement of between $140.0 million and $639.0 million, with a mean and median of upfront consideration of $289.3 million and $200.0 million, respectively. Cantor then compared the implied equity values attributable to the 3.1% of the combined company to be held immediately following the Merger by holders of Signal common stock at the time of Cantor s opinion of approximately $9.0 million and $6.2 million based on the mean and median, respectively, upfront consideration paid in the Selected Transactions to Signal s estimated liquidation value, per Signal management, of negative $559,000.

General

Cantor acted as a financial advisor to Signal in connection with the Merger and Signal agreed to pay Cantor a fee of approximately $750,000, $250,000 of which was paid upon delivery of Cantor s opinion. In addition, Signal agreed to reimburse Cantor for certain expenses and to indemnify Cantor against certain liabilities arising out of its engagement.

Cantor had been engaged during the two years preceding the date of its opinion by Signal to provide certain investment banking and other services on matters unrelated to the Merger, for which it has received fees of approximately $178,000. Cantor may seek to provide Signal and its affiliates with certain investment banking and other services unrelated to the Merger in the future.

Consistent with applicable legal and regulatory requirements, Cantor adopted certain policies and procedures to establish and maintain the independence of Cantor s research departments and personnel. As a result, Cantor s research analysts may hold views, make statements or investment recommendations and/or publish research reports with respect to Signal, the Merger and other participants in the Merger that differ from the views of Cantor s investment banking personnel.

In the ordinary course of business, Cantor and its affiliates may actively trade (for their own accounts and for the accounts of their customers) certain equity and debt securities, bank debt and/or other financial instruments

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issued by Signal and affiliates, as well as derivatives thereof, and, accordingly, may at any time hold long or short positions in such securities, bank debt, financial instruments and derivatives.

Interests of the Signal Directors and Executive Officers in the Merger

In considering the recommendation of Signal s board of directors with respect to issuing shares of Signal common stock as contemplated by the Merger Agreement and the other matters to be acted upon by Signal stockholders at the Signal special meeting, Signal stockholders should be aware that certain members of the board of directors and executive officers of Signal have interests in the Merger that may be different from, or in addition to, the interests of Signal stockholders. These interests relate to or arise from the matters described below. The board of directors of each of Signal and Miragen were aware of these potential conflicts of interest and considered them, among other matters, in reaching their respective decisions to approve the Merger Agreement and the Merger, and to recommend, as applicable, that the Signal stockholders approve the Signal proposals to be presented to the Signal stockholders for consideration at the Signal special meeting as contemplated by this proxy statement/prospectus/information statement, and that the Miragen stockholders sign and return the written consent as contemplated by this proxy statement/prospectus/information statement.

Severance and Bonus Payments

Under the original terms of the employment agreements for each of Samuel D. Riccitelli, Signal s president and chief executive officer, and Tamara A. Seymour, Signal s chief financial officer, upon the executive s termination without Cause, or in connection with executive s resignation for Good Reason, each as defined in the employment agreements, each executive officer was eligible to receive continued base salary payments (less all applicable withholdings) and COBRA premium payments for twelve months following termination payable each month in monthly installments over the applicable period in accordance with Signal s payroll period. Neither executive officer was required to mitigate the amount of any severance payments received by seeking other employment during the term of his or her severance period. However, if the executive officer were to obtain other employment during the term of the severance period, Signal would have only needed to pay such executive officer, for the remaining length of the severance period, the difference between such executive officer s new salary and base salary (as in effect at the time of termination), if the new salary is less than such executive officer s base salary (i.e., Signal would not have been obligated to make any severance payments to such executive officer if his or her new salary was greater than his or her applicable base salary). Signal was also obligated to reimburse each executive officer for premiums for COBRA coverage for the applicable executive officer (and to the extent he or she has family coverage, his or her family), provided such executive officer elects such coverage, during the applicable period when such executive officer is receiving severance payments, until such time as such executive officer obtains other employment and is entitled to comparable health coverage from his or her new employer.

The employment of Mr. Riccitelli and Ms. Seymour is expected to terminate no later than the consummation of the Merger. The compensation committee of the board of directors deemed it advisable and in the best interests of Signal stockholders to permit lump sum payment of the severance arrangements of Mr. Riccitelli and Ms. Seymour upon his or her termination to the extent permitted under Section 409A of the Code, as opposed to the monthly payments originally contemplated therein to avoid a potential acquirer from having to make continued payments following the closing of a merger. Therefore, on October 11, 2016, the compensation committee of Signal s board of directors approved modifications to the severance arrangements of Mr. Riccitelli and Ms. Seymour to allow for the payment of severance in a lump sum to the extent such payments can be made in compliance with Section 409A of the Code.

2015 Bonus Payments

The employment agreements for Mr. Riccitelli and Ms. Seymour allow for annual incentive compensation bonus payments to be awarded in the sole discretion of the compensation committee of Signal s board of directors. The

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incentive compensation for Mr. Riccitelli may be paid on the terms established from time to time by the compensation committee of Signal and Ms. Seymour is eligible to receive a bonus payment of up to 30% of her base salary then in effect, which bonus payment will be awarded in the sole discretion of the compensation committee based upon performance goals established by the compensation committee and paid subject to her continued employment through the date of payment.

On March 28, 2016, the compensation committee of Signal s board of directors approved bonuses for Mr. Riccitelli and Ms. Seymour of up to $135,000 and $105,000, respectively, for the 2015 performance of such executive officers. Of the awarded amounts, $33,750 and $26,250 were paid to Mr. Riccitelli and Ms. Seymour, respectively, in April 2016. The remainder of these amounts, consisting of $101,250 for Mr. Riccitelli and $78,750 for Ms. Seymour would be paid upon the completion of a strategic transaction of Signal and subject to the availability of funds. On October 11, 2016, the compensation committee of Signal s board of directors approved the payment of the remainder of such bonuses to Mr. Riccitelli and Ms. Seymour of $101,250 and $78,750, respectively, upon the closing of the Merger.

2016 Bonus Payments

As discussed above, incentive compensation for Mr. Riccitelli may be paid on the terms established from time to time by, and at the discretion of, the compensation committee of Signal, and Ms. Seymour is eligible to receive a bonus payment of up to 30% of her base salary then in effect. Such bonus payments are awarded in the sole discretion of the compensation committee based upon performance goals established by the compensation committee. In the event the compensation committee determines that funds are available to provide for the payment of incentive compensation bonus payments for the 2016 performance of Mr. Riccitelli and Ms. Seymour, Mr. Riccitelli and Ms. Seymour are eligible to receive an amount to be determined by the compensation committee. If approved by the compensation committee of Signal s board of directors, the bonus amounts are expected to be $178,200 for Mr. Riccitelli and $138,600 for Ms. Seymour, and will be paid upon closing of the Merger.

Acceleration of Unvested RSU Awards

The restricted stock unit awards held by the executive officers allowed for vesting acceleration in full upon a Change in Control of Signal, as such term is defined in the 2014 Stock Incentive Plan of Signal. As contemplated under the Merger Agreement, the lab business of Signal is expected to be wound down or sold prior to the closing of the Merger. Therefore, the compensation committee of the board of directors recognized that holders of restricted stock unit awards may be terminated prior to the closing of the Merger, or a deemed Change in Control under the 2014 Stock Incentive Plan, without obtaining the benefit of their restricted stock unit awards. Therefore, on October 11, 2016, the compensation committee of the board of directors approved the acceleration in full of the unvested portions of the restricted stock unit awards held by the executive officers, subject to the signing of the Merger Agreement and the signing of a non-binding letter of intent for the sale of Signal s lab business. The acceleration in full of such unvested portions of such restricted stock unit awards occurred as of the business day prior to the signing of the Merger Agreement on October 28, 2016.

Acceleration of Unvested Option Awards

On October 11, 2016, the compensation committee of Signal s board of directors approved the acceleration in full of the unvested portions of the stock options held by the Signal directors and Ms. Seymour in connection with the signing of the Merger Agreement. All stock option awards held by Ms. Seymour are currently out-of-the-money. As of December 31, 2016, all vested stock options to purchase shares of common stock held by Signal directors were out-of-the-money.

Named Executive Officer Compensation

The following table and the related footnotes present information about the compensation payable to Signal s named executive officers included in Signal s most recent filing under the Exchange Act that required disclosure

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pursuant to Item 402(c) of Regulation S-K. The compensation shown in the table below is intended to comply with Item 402(t) of Regulation S-K, which requires disclosure of information about compensation for each named executive officer that is based on or otherwise relates to the Merger.

The named executive officers are not entitled to any pension or non-qualified deferred compensation benefits enhancements or any tax reimbursements in connection with the Merger. Further, all stock options held by the named executive officers of Signal are currently out-of-the-money.

Golden Parachute Compensation

Name	Cash(1)	Perquisites/ Benefits(2)	Other(3)	Total
Samuel D. Riccitelli	$ 551,250	$ 26,762	$ 178,200	$ 756,212
Tamara A. Seymour	$ 428,750	$ 9,880	$ 138,600	$ 577,230

(1) The amount in this column for Mr. Riccitelli represents $450,000 in severance payments and reflects the $101,250 remaining payment under his 2015 performance bonus described above under Severance and Bonus Payments. The amount in this column for Ms. Seymour represents $350,000 in severance payments and reflects the $78,750 remaining payment under her 2015 performance bonus described above under Severance and Bonus Payments.

(2) The amounts in this column reflect 12 months of health insurance premium payments for Mr. Riccitelli and 12 months of health insurance premium payments for Ms. Seymour.

(3) The amount in this column represents an estimated amount of cash payments Mr. Riccitelli and Ms. Seymour are eligible to receive pursuant to Signal s incentive bonus program for 2016 described above under Severance and Bonus Payments. Payments under Signal s incentive bonus program are paid in the sole discretion of the compensation committee of the board of directors. To date, the compensation committee has not approved the payment of any such payments for the 2016 performance of such executive officers.

Amendment to the Bennet S. Lebow Promissory Note

On March 6, 2015, Signal originally issued the Note to Bennett S. LeBow, a member of Signal s Board of Directors and Signal s largest stockholder. When issued, the terms of the Note provided (i) for a principal amount of $1,105,009, which accrued interest computed on the basis of the actual number of days elapsed in a 360-day year, at a rate per annum of 8%, (ii) that at any time on or after June 30, 2015, Mr. LeBow may demand payment of the entire outstanding principal of the Note and all unpaid interest accrued thereon and (iii) that upon the occurrence and during the continuance of any event of default by Signal under the Note, the principal balance of the Note shall accrue interest at a rate of 11%.

Given its cash position, Signal would have difficulty operating its business until the closing of a potential merger with a net positive cash position and repaying the outstanding amount due under the Note with Mr. LeBow. Therefore, on October 31, 2016, the board of directors deemed it advisable and in the best interests of Signal stockholders to approve the Note Amendment.

On October 31, 2016, prior to the execution of the Merger Agreement, Signal and Mr. LeBow entered into the Note Amendment. The Note Amendment (i) makes the outstanding principal balance and all accrued interest on the Note, plus a premium of 11% on the outstanding balance, automatically convertible into shares of Signal s common stock

immediately prior to the effective time of the Merger at a conversion price of $5.39 per share, which is the closing price of Signal s common stock on the effective date of the Note Amendment, after giving effect to Signal s one-for-15 reverse stock split effected on November 4, 2016, and (ii) modifies the principal amount of the Note to $1,045,000, the original amount advanced to Signal as of June 17, 2014, and the interest of the Note to a rate per annum of 11% commencing on June 17, 2014, with interest computed on the basis of the actual number of days in a 360-day year.

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The conversion price is subject to appropriate adjustment in the event of any reverse stock split, forward stock split, stock dividend, combination or other similar recapitalization with respect to Signal s common stock. Conversion of the Note is subject to and conditioned upon Signal obtaining stockholder approval of any such conversion.

If conversion of the Note is not approved by Signal stockholders at the special meeting, or if the Merger Agreement is terminated prior to completion of the Merger, the outstanding balance due under the Note will not be converted into Signal common stock and the Note will remain outstanding. Moreover, because conversion of the outstanding balance of the Note into shares of Signal common stock is a closing condition of the Merger Agreement, success of the Merger is also dependent upon stockholder approval of conversion of the Note.

Ownership Interests

As of December 31, 2016, directors and executive officers of Signal owned or controlled 26% of the outstanding shares of Signal common stock. Signal directors and executives have entered into support agreements in connection with the Merger. For a more detailed discussion of the support agreements see the section titled *Agreements Related to the Merger Support Agreements* in this proxy statement/prospectus/information statement.

Indemnification and Insurance for the Signal Officers and Directors

Under the Merger Agreement, from the closing of the Merger through the sixth anniversary of the closing, Signal and the surviving corporation agree that all rights to indemnification, exculpation or advancement of expenses now existing in favor of, and all limitations on the personal liability of, each present and former director or officer, of Signal or Miragen provided for in the respective organizational documents of Miragen and Signal in effect as of October 31, 2016, shall continue to be honored and in full force and effect.

Under the Merger Agreement, the certificate of incorporation and bylaws of Signal and the surviving corporation in the Merger, will contain provisions no less favorable with respect to indemnification, advancement of expenses and exculpation of present and former directors and officers of each of Signal and Miragen than are presently set forth in the certificate of incorporation and bylaws of Signal and Miragen, as applicable, which provisions shall not be amended, modified or repealed for a period of six years time from the closing of the Merger in a manner that would materially and adversely affect the rights thereunder of individuals who, at or prior to the closing, were officers or directors of Signal and Miragen.

The Merger Agreement also provides that Signal shall purchase an insurance policy in effect for six years from the closing, providing at least the same coverage as the current directors and officers liability insurance policies maintained by Miragen and Signal and containing terms and conditions that are not materially less favorable to current and former officers and directors of Miragen and Signal.

Interests of Miragen Directors and Executive Officers in the Merger

In considering the recommendation of Miragen s board of directors with respect to adopting the Merger Agreement, Miragen stockholders should be aware that certain members of the board of directors and executive officers of Miragen have interests in the Merger that may be different from, or in addition to, interests they may have as Miragen stockholders. Miragen s board of directors was aware of these potential conflicts of interest and considered them, among other matters, in reaching their respective decisions to approve the Merger Agreement, the Merger and related transactions, and to recommend that the Miragen stockholders sign and return the written consent as contemplated by this proxy statement/prospectus/information statement.

Ownership Interests

Some of Miragen s directors and executive officers currently hold shares of Miragen s common stock or shares of convertible preferred stock, of which each share will convert into one share of Miragen common stock prior to

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the closing of the Merger. Each one share of Series A convertible preferred stock, Series B convertible preferred stock and Series C convertible preferred stock converts into one share of common stock. The table below sets forth the anticipated ownership of Miragen s common stock by Miragen s directors and executive officers immediately prior to the closing of the Merger based on their ownership of Miragen s capital stock as of December 31, 2016, without giving effect to any shares of common stock that each director, executive officer or any affiliates thereof may purchase in Miragen s concurrent financing in connection with the Merger.

Stockholder Name	Number of Shares of Miragen Common Stock Immediately Prior to the Closing of the Merger
William S. Marshall, Ph.D.(1)	211,319
Jason A. Leverone(2)	
Adam S. Levy(3)	
Paul D. Rubin, M.D.(4)	
Bruce L. Booth, Ph.D.(5)	
Reza Halse, Ph.D.(6)	
John W. Creecy(7)	
Thomas E. Hughes, Ph.D.(8)	20,000
Kyle A. Lefkoff (9)	
Kevin Koch, Ph.D.(10)	
Joseph L. Turner(11)	

(1) Consists of 150,000 shares of common stock, 37,586 shares of Series A convertible preferred stock, 6,470 shares of Series B convertible preferred stock and 17,263 shares of Series C convertible preferred stock. Dr. Marshall is Miragen s president and chief executive officer and a member of its board of directors. For additional information regarding shares of Miragen s common stock issuable to Dr. Marshall upon exercise of outstanding options, please see the table below.

(2) Mr. Leverone is Miragen s chief financial officer. For additional information regarding shares of Miragen s common stock issuable to Mr. Leverone upon exercise of outstanding options, please see the table below.

(3) Mr. Levy is Miragen s chief business officer. For additional information regarding shares of Miragen s common stock issuable to Mr. Levy upon exercise of outstanding options, please see the table below.

(4) Dr. Rubin is Miragen s executive vice president, research and development. For additional information regarding shares of Miragen s common stock issuable to Dr. Rubin upon exercise of outstanding options, please see the table below.

(5) Dr. Booth is a member of Miragen s board of directors and a director of Atlas Venture Associates VII, Inc., which is the general partner of Atlas Venture Associates VII, L.P. which is the general partner of Atlas Venture VII, L.P., with each referred to as an Atlas Entity and, collectively, the Atlas Entities. For additional information regarding ownership of Miragen capital stock by the Atlas Entities, please see the table below.

(6) Dr. Halse is a member of Miragen s board of directors and a partner of MRL Ventures Fund, LLC. For additional information regarding ownership of Miragen capital stock by MRL Ventures Fund, LLC, please see the table below. Dr. Halse has informed Miragen that he will resign as a member of Miragen s board of directors immediately prior to the effectiveness of the Merger.

(7) Mr. Creecy is a member of Miragen s board of directors and the chief executive officer of Remeditex Ventures LLC. For additional information regarding ownership of Miragen capital stock by Remeditex Ventures LLC, please see the table below.

(8) Consists of 20,000 shares of common stock. Dr. Hughes is a member of Miragen s board of directors. For additional information regarding shares of Miragen s common stock issuable to Dr. Hughes upon exercise of outstanding options, please see the table below.

(9) Mr. Lefkoff is a member of Miragen s board of directors and a managing member of BV Partners VI, L.L.C., which is the general partner of Boulder Ventures VI, L.P., and a managing member of BV

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Partners V, L.L.C., which is the general partner of Boulder Ventures V, L.P., with each referred to as a BV Entity and, collectively, the BV Entities. For additional information regarding ownership of Miragen capital stock by the BV Entities, please see the table below.

(10) Mr. Koch is a member of Miragen s board of directors. For additional information regarding shares of Miragen s common stock issuable to Mr. Koch upon exercise of outstanding options, please see the table below.

(11) Mr. Turner is designated by Miragen to be appointed as a member of the combined company s board of directors effective as of the closing of the Merger.

Some of Miragen s other stockholders affiliated with Miragen s directors also currently hold shares of Miragen s common stock or shares of convertible preferred stock, of which each share will convert into one share of Miragen common stock prior to the closing of the Merger. The table below sets forth the anticipated ownership of Miragen s common stock by other affiliates of Miragen s directors immediately prior to the closing of the Merger based on their ownership of Miragen s capital stock as of December 31, 2016, without giving effect to any shares of common stock that stockholder may purchase in Miragen s concurrent financing in connection with the Merger.

Stockholder Name	Number of Shares of Miragen Common Stock Immediately Prior to the Closing of the Merger
Atlas Entities(1)	4,469,607
Remeditex Ventures LLC(2)	3,052,163
BV Entities(3)	2,850,548
MRL Ventures Fund, LLC(4)	1,580,135

(1) Consists of 83,250 shares of common stock, 2,661,454 shares of Series A convertible preferred stock, 479,401 shares of Series B convertible preferred stock and 1,245,502 shares of Series C convertible preferred stock. All shares are held directly by Atlas Venture VII, L.P., or Atlas Venture VII. Atlas Venture Associates VII, L.P., or AVA VII LP, is the general partner of Atlas Venture VII, and Atlas Venture Associates VII, Inc., or AVA VII Inc., is the general partner of AVA VII LP. Peter Barrett, Bruce L. Booth, Ph.D., Jean-Francois Formela and Jeff Fagnan is each a director of AVA VII Inc. Dr. Booth is a member of Miragen s board of directors.

(2) Consists of 1,083,333 shares of Series B Preferred Stock and 1,968,830 shares of Series C convertible preferred stock. All shares are held directly by Remeditex Ventures LLC, or Remeditex. John H. Creecy is the chief executive officer of Remeditex and may be deemed to be the indirect beneficial owner of the shares owned by Remeditex. Mr. Creecy is a member of Miragen s board of directors.

(3) Consists of 55,500 shares of common stock, 1,691,598 shares of Series A convertible preferred stock, 306,027 shares of Series B convertible preferred stock and 797,423 shares of Series C convertible preferred stock. Includes shares held by Boulder Ventures V, L.P., or Boulder Ventures V, and shares held by Boulder Ventures VI, L.P., or Boulder Ventures VI and, collectively with Boulder Ventures V, the Boulder Ventures Funds. BV Partners V, L.L.C., or BV V, is the general partner of Boulder Ventures V. BV Partners VI, L.L.C., or BV VI, is the general partner of Boulder Ventures VI. BV V may be deemed to indirectly beneficially own the shares owned by Boulder Ventures V and BV VI may be deemed to indirectly beneficially own the shares owned by Boulder Ventures VI. Kyle A. Lefkoff, Peter A. Roshko and Jonathan L. Perl are managing members of BV V and Mr. Lefkoff, Mr. Roshko and Mr. Perl are managing members of BV VI. Mr. Lefkoff is a member of Miragen s board of directors.

(4) Consists of 1,580,135 shares of Series C convertible preferred stock. All shares are held directly by MRL Ventures Fund, LLC, or MRL Ventures. Reza Halse is a partner of MRL Ventures and may be deemed to be the indirect beneficial owner of the shares owned by MRL Ventures. Dr. Halse is a member of Miragen s board of directors. Dr. Halse has informed Miragen that he will resign as a member of Miragen s board of directors immediately prior to the effectiveness of the Merger.

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Stock Options

Two of Miragen s directors, Dr. Hughes and Mr. Koch, and Miragen s executive officers hold options to purchase shares of Miragen common stock, which, pursuant to the Merger Agreement, will be converted into and become options to purchase shares of Signal common stock. In connection with the conversion of the options, the number of shares subject to the options and the option exercise prices will be adjusted pursuant to the terms of the Merger Agreement. The number of shares subject to each option will be multiplied by the Exchange Ratio, rounding any resulting fractional shares down to the nearest whole share, and the exercise price of each option will be divided by the Exchange Ratio, rounding up to the nearest whole cent. The option terms will remain the same, including any vesting terms. The table below sets forth certain information with respect to the options.

Optionholder Name	Grant Date	Expiration Date	Exercise Price ($)	Number of Shares of Common Stock Underlying Option as of December 31, 2016	Number Vested as of December 31, 2016
William S. Marshall, Ph.D.	7/31/2008	7/30/2018	0.40	164,726	164,726
	6/15/2012	6/14/2022	0.86	328,500	328,500
	2/22/2016	2/21/2016	0.74	223,000	46,458
Jason A. Leverone	12/10/2008	12/09/2018	0.40	42,000	42,000
	9/24/2009	9/23/2019	0.40	4,400	4,400
	3/16/2010	3/15/2020	0.40	16,000	16,000
	6/15/2012	6/14/2022	0.86	66,300	66,300
	2/22/2016	2/21/2026	0.74	50,000	10,416
Adam S. Levy	6/15/2016	6/14/2026	0.74	230,883	0
Paul D. Rubin	11/30/2016	11/29/2026	4.00	288,604	0
Thomas E. Hughes, Ph.D.	6/15/2012	6/14/2022	0.86	16,000	16,000
	2/22/2016	2/21/2026	0.74	19,500	4,875
Kevin Koch, Ph.D.	8/18/2016	8/17/2026	0.74	41,600	3,466

Private Placement of Common Stock.

In October 2016, Miragen entered into the Subscription Agreement with certain current stockholders of Miragen and certain new investors in Miragen pursuant to which the purchasers agreed to purchase an aggregate of 9,045,126 shares of Miragen s common stock at a price per share of $4.50 for an aggregate consideration of approximately $40.7 million immediately prior to, and conditioned upon, the consummation of the Merger. The table below sets forth the number of shares of Miragen s common stock agreed to be purchased and the purchase price for the shares of common stock for each purchaser that is a director or executive officer of Miragen or are their affiliates.

Name of Purchaser	Shares of Common Stock	Purchase Price ($)

	(#)	
Atlas Venture Fund X, L.P.(1)	1,145,835	$ 5,156,257.50
Boulder Ventures VI, L.P.(2)	147,419	$ 663,385.50
MRL Ventures Fund, LLC (3)	412,774	$ 1,857,483.00
Remeditex Ventures LLC(4)	797,308	$ 3,587,886.00

(1) The Atlas Entities, together, hold more than 5% of Miragen s outstanding capital stock. Bruce L. Booth is a member of Miragen s board of directors and a director of Atlas Venture Associates VII, Inc. and Atlas Venture Associates X, Inc., which are affiliated with the Atlas Entities.

(2) Boulder Ventures holds more than 5% of Miragen s outstanding capital stock. Kyle A. Lefkoff is a member of Miragen s board of directors and a managing member of BV Partners V, L.L.C. and BV Partners VI, L.L.C., which are each affiliated with Boulder Ventures.

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(3) MRL Ventures Fund, LLC holds more than 5% of Miragen s outstanding capital stock. Reza Halse is a member of Miragen s board of directors and a partner MRL Ventures Fund, LLC. Dr. Halse has informed Miragen that he will resign as a member of Miragen s board of directors immediately prior to the effectiveness of the Merger.
(4) Remeditex Ventures LLC holds more than 5% of Miragen s outstanding capital stock. John H. Creecy is a member of Miragen s board of directors and the chief executive officer of Remeditex Ventures LLC.

Management Following the Merger

As described elsewhere in this joint proxy statement/prospectus/information statement, including in *Management Following the Merger* beginning on page 247, Miragen s directors and executive officers are expected to become directors and executive officers of the combined company upon the closing of the Merger.

Employment Agreements

As described elsewhere in this joint proxy statement/prospectus/information statement, including in *Management Following the Merger Executive Compensation Employment Agreements and Potential Payments Upon Termination of Employment or Change in Control* beginning on page 258, Miragen s executive officers are party to employment agreements which become effective only upon closing of the Merger.

Indemnification and Insurance for the Miragen Officers and Directors

Under the Merger Agreement, from the closing of the Merger through the sixth anniversary of the closing, Signal and the surviving corporation agree that all rights to indemnification, exculpation or advancement of expenses now existing in favor of, and all limitations on the personal liability of, each present and former director or officer, of Signal or Miragen provided for in the respective organizational documents of Miragen and Signal in effect as of October 31, 2016, shall continue to be honored and in full force and effect.

Under the Merger Agreement, the certificate of incorporation and bylaws of Signal and the surviving corporation in the Merger, will contain provisions no less favorable with respect to indemnification, advancement of expenses and exculpation of present and former directors and officers of each of Signal and Miragen than are presently set forth in the certificate of incorporation and bylaws of Signal and Miragen, as applicable, which provisions shall not be amended, modified or repealed for a period of six years time from the closing of the Merger in a manner that would materially and adversely affect the rights thereunder of individuals who, at or prior to the closing, were officers or directors of Signal and Miragen.

The Merger Agreement also provides that Signal shall purchase an insurance policy in effect for six years from the closing, providing at least the same coverage as the current directors and officers liability insurance policies maintained by Miragen and Signal and containing terms and conditions that are not materially less favorable to current and former officers and directors of Miragen and Signal.

Limitations on Liability and Indemnification.

In addition to the indemnification required in the Merger Agreement, Miragen has entered into indemnification agreements with each of its directors and executive officers. These agreements provide for the indemnification of the directors and executive officers of Miragen 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 agents of Miragen. Miragen anticipates that the directors and officers of the combined company will enter into substantially similar agreements with the combined company, effective upon consummation of the Merger.

Form of the Merger

The Merger Agreement provides that at the effective time, Merger Sub will be merged with and into Miragen. Upon the consummation of the Merger, Miragen will continue as the surviving corporation and will be a wholly-owned subsidiary of Signal.

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After completion of the Merger, assuming Signal Proposal No. 6 is approved by Signal stockholders at the Signal special meeting, Signal will be renamed Miragen Therapeutics, Inc. and expects to trade on The NASDAQ Capital Market under the symbol MGEN.

Merger Consideration and Exchange Ratio

Immediately prior to the effective time of the Merger, each outstanding shares of preferred stock of Miragen will be converted into common stock. At the effective time of the Merger:

- each outstanding share of common stock of Miragen will be converted into the right to receive that number of shares of Signal common stock as determined pursuant to the Exchange Ratio described in more detail below;
- each outstanding option to purchase shares of Miragen common stock will be assumed by Signal and will be converted into an option to purchase shares of Signal common stock; and
- each outstanding warrant to purchase shares of Miragen capital stock will be assumed by Signal and will be converted into a warrant to purchase shares of Signal common stock.

No fractional shares of Signal common stock will be issued in connection with the Merger. Instead, each Miragen stockholder who otherwise would be entitled to receive a fractional share of Signal common stock (after aggregating all fractional shares of Signal common stock issuable to such holder) will be entitled to receive an amount in cash representing such holder s proportionate interest, if any, in the proceeds from the sale of the aggregated fractional shares by the exchange agent (reduced by any fees of the exchange agent attributable to such sale) at the then prevailing prices on the NASDAQ Capital Market.

The Exchange Ratio is calculated using a formula intended to allocate existing Miragen securityholders (on a fully-diluted basis), a percentage of the combined company. Based on Miragen s and Signal s capitalization as of December 31, 2016, the Exchange Ratio is estimated to be (i) approximately 0.6995 pre-split shares of Signal common stock, subject to adjustment to account for the effect of a reverse stock split of Signal common stock, within a range of one new share for every one to 15 shares outstanding, to be implemented prior to the consummation of the Merger as discussed in this proxy statement/prospectus/information statement or (ii), post-split, between approximately 0.6995 and 0.0466 shares of Signal common stock. These estimates are subject to adjustment prior to closing of the Merger, including (i) adjustments to account for the issuance of any additional shares of Miragen or Signal common stock, as applicable, prior to the consummation of the Merger, provided that, the issuance of Miragen common stock in the concurrent financing will not impact the Exchange Ratio, or (ii) an upward adjustment to the extent that Signal s net cash at the effective time of the Merger is less than negative $100,000 (and as a result, Signal securityholders could own less, and Miragen securityholders could own more, of the combined company).

Based on the estimates set forth above, immediately after the Merger, Miragen securityholders would own approximately 96% of the fully-diluted common stock of the combined company and Signal securityholders would own approximately 4% of the fully-diluted common stock of the combined company, each assuming that Miragen closes its concurrent financing immediately prior to the effective time of the Merger. If the concurrent financing does not close, then Miragen securityholders would own approximately 94% of the fully-diluted common stock of the combined company and Signal securityholders would own approximately 6% of the fully-diluted common stock of the

combined company.

The Exchange Ratio formula is the quotient obtained by dividing the number of Miragen merger shares (defined below) by the Miragen fully-diluted outstanding shares (defined below), where:

Miragen merger shares is the product determined by ***multiplying*** (i) the post-closing Signal shares *by* (ii) the Miragen allocation percentage.

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Miragen fully-diluted outstanding shares is the total number of shares of Miragen common stock outstanding immediately prior to the effective time of the Merger on a fully-diluted and an as-converted to common stock basis, assuming the exercise of each outstanding Miragen option and Miragen warrant to purchase Miragen capital stock and the effectiveness of the conversion of all of Miragen s outstanding preferred stock into Miragen common stock; provided, however, that all shares of Miragen common stock issued in its concurrent financing will be excluded from such amount.

Post-closing Signal shares is the quotient determined by *dividing (i) the Signal fully-diluted outstanding shares by* (ii) the Signal allocation percentage.

Signal fully-diluted outstanding shares is the total number of shares of Signal common stock outstanding immediately prior to the effective time of the Merger on a fully-diluted and an as-converted to common stock basis, assuming (i) the exercise of each outstanding Signal option to purchase Signal common stock (to the extent such option will not be cancelled pursuant to the Merger Agreement), (ii) the settlement in shares of Signal common stock of each outstanding Signal restricted stock unit (to the extent such restricted stock until will not be cancelled pursuant to the Merger Agreement), (iii) the exercise of each outstanding Signal warrant to purchase common stock, and (iv) the conversion of the indebtedness into Signal common stock in accordance with the terms and conditions of the Note Amendment.

Miragen allocation percentage is 1.00 *minus* the Signal allocation percentage.
Signal allocation percentage is 0.06; *provided, however, solely* to the extent that the net cash determined pursuant to the Merger Agreement is less than negative $100,000, then 0.06 shall be reduced by 0.00000002 for each $1.00 that the Net Cash as so determined is less than negative $100,000 (for example, the Signal allocation percentage would be 0.055 if Signal s net cash is negative $350,000).

Stock Options and Warrants

All warrants to purchase shares of Signal s common stock that are outstanding immediately prior to the effective time of the Merger will remain outstanding following the effective time of the Merger. All options to purchase shares of Signal common stock and restricted stock units that are not exercised or settled, as applicable, prior to the effective time will be cancelled and terminated upon the effectiveness of the Merger.

At the effective time of the Merger, each outstanding option and warrant, whether or not vested, to purchase shares of Miragen capital stock unexercised immediately prior to the effective time of the Merger will be converted into an option or warrant to purchase shares of Signal common stock. All rights with respect to each Miragen option or warrant will be assumed by Signal in accordance with its terms. Accordingly, from and after the effective time of the Merger each option or warrant assumed by Signal may be exercised solely for shares of Signal common stock.

The number of shares of Signal common stock subject to each outstanding Miragen option or warrant assumed by Signal will be determined by multiplying the number of shares of Miragen capital stock that were subject to such option or warrant, as applicable, by the Exchange Ratio and rounding the resulting number down to the nearest whole number of shares of Signal common stock. The per share exercise price for the shares of Signal common stock issuable upon exercise of each Miragen option or warrant assumed by Signal will be determined by dividing the per share exercise price of Miragen capital stock subject to such option or warrant, as applicable, by the Exchange Ratio and rounding the resulting exercise price up to the nearest whole cent. Any restriction on the exercise of any option or

warrant will continue in full force and effect and the term, exercisability, vesting schedule and other provisions of such option or warrant will otherwise remain unchanged.

Effective Time of the Merger

The Merger Agreement requires the parties to consummate the Merger after all of the conditions to the consummation of the Merger contained in the Merger Agreement are satisfied or waived, including the approval

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by the Signal stockholders of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9. The Merger will become effective upon the filing of a certificate of Merger with the Secretary of State of the State of Delaware or at such later time as is agreed by Signal and Miragen and specified in the certificate of Merger. Neither Signal nor Miragen can predict the exact timing of the consummation of the Merger.

Regulatory Approvals

Signal must comply with applicable federal and state securities laws and the rules and regulations of The NASDAQ Capital Market in connection with the issuance of shares of Signal common stock and the filing of this proxy statement/prospectus/information statement with the SEC.

Tax Treatment of the Merger

Signal and Miragen intend the Merger to qualify as a reorganization within the meaning of Section 368(a) of the Internal Revenue Code of 1986, as amended, or the Code. Each of Signal and Miragen will use its commercially reasonable efforts to cause the Merger to qualify as a reorganization within the meaning of Section 368(a) of the Code, and not to permit or cause any affiliate or any subsidiary of Signal or Miragen to, take any action or cause any action to be taken which would cause the Merger to fail to qualify as a reorganization under Section 368(a) of the Code. For a description of material U.S. federal income tax consequences of the Merger, see the section titled *The Merger Material U.S. Federal Income Tax Consequences of the Merger* below.

Material U.S. Federal Income Tax Consequences of the Merger

The following is a discussion of material U.S. federal income tax consequences of the Merger applicable to U.S. Holders (as defined below) who exchange their Miragen common stock for Signal common stock in the Merger assuming the Merger is consummated as contemplated herein. 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 Code, U.S. Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the Internal Revenue Service, or the IRS, each as in effect as of the date of the Merger. These authorities are subject to differing interpretations or change. Any such change, which may or may not be retroactive, could alter the tax consequences to holders of Miragen common stock as described herein.

This discussion does not address all U.S. federal income tax consequences relevant to the particular circumstances of a Miragen common stockholder. In addition, it does not address consequences relevant to holders of Miragen common stock that are subject to particular U.S. or non-U.S. tax rules, including, without limitation:

- persons who hold their Miragen common stock in a functional currency other than the U.S. dollar;
- persons who hold Miragen common stock that constitutes qualified small business stock under Section 1202 of the Code or as Section 1244 stock for purposes of Section 1244 of the Code;
- persons holding Miragen common stock as part of an integrated investment (including a straddle, pledge against currency risk, constructive sale or conversion transaction or other integrated or risk reduction transactions) consisting of shares of Miragen common stock and one or more other positions;

persons who are not U.S. Holders as defined below;

banks, insurance companies, mutual funds, tax-exempt entities, financial institutions, broker-dealers, real estate investment trusts or regulated investment companies;

persons who do not hold their Miragen common stock as a capital asset within the meaning of Section 1221 of the Code;

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partnerships or other entities classified as partnerships or disregarded entities for U.S. federal income tax purposes, S corporations or other pass-through entities (including hybrid entities);

persons who acquired their Miragen common stock pursuant to the exercise of compensatory options or in other compensatory transactions;

persons who acquired their Miragen common stock pursuant to the exercise of warrants or conversion rights under convertible instruments;

persons holding Miragen common stock who exercise dissenters rights;

persons who acquired their Miragen common stock in a transaction subject to the gain rollover provisions of Section 1045 of the Code; and

persons who hold their Miragen common stock through individual retirement accounts or other tax-deferred accounts.

For purposes of this discussion, a U.S. Holder is a beneficial owner of Miragen common stock that, for U.S. federal income tax purposes, is or is treated as:

an individual who is a citizen or resident of the United States;

a corporation (or other entity taxable as a corporation for U.S. federal income tax purposes) created or organized in or 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 taxation regardless of its source; or

a trust if either (i) a court within the United States is able to exercise primary supervision over the administration of such trust and one or more United States persons (within the meaning of Section 7701(a)(30) of the Code) are authorized or have the authority to control all substantial decisions of such trust, or (ii) the trust was in existence on August 20, 1996 and has a valid election in effect under applicable Treasury Regulations to be treated as a United States person for U.S. federal income tax purposes.

If an entity treated as a partnership for U.S. federal income tax purposes holds Miragen 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. If you are a partnership or a partner of a partnership holding Miragen common stock or any other person excluded from this discussion, you should consult your tax advisor regarding the tax consequences of the Merger.

In addition, the following discussion does not address (i) any U.S. federal non-income tax consequences of the Merger, including estate, gift or other tax consequences, (ii) any state, local or non-U.S. tax consequences of the Merger, (iii) the Medicare contribution tax on net investment income or the alternative minimum tax, (iv) the tax consequences of transactions effectuated before, after or at the same time as the Merger (whether or not they are in connection with the Merger), including, without limitation, transactions in which Miragen common stock is acquired (including, but not limited to, pursuant to the Subscription Agreement) or Miragen preferred stock is converted to Miragen common stock, and (v) the tax consequences to holders of options, warrants or similar rights to purchase Miragen common stock.

IN LIGHT OF THE FOREGOING, HOLDERS OF MIRAGEN COMMON STOCK SHOULD CONSULT THEIR OWN TAX ADVISORS REGARDING THE TAX CONSEQUENCES TO THEM OF THE MERGER, INCLUDING THE APPLICABLE U.S. FEDERAL, STATE, LOCAL AND NON-U.S. INCOME AND OTHER TAX CONSEQUENCES, AND ANY TAX REPORTING REQUIREMENTS OF THE MERGER AND RELATED TRANSACTIONS IN LIGHT OF THEIR PARTICULAR CIRCUMSTANCES.

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In connection with the filing of the registration statement of which this proxy statement/prospectus/information statement is a part, Pillsbury will deliver to Signal and Cooley will deliver to Miragen opinions that the statements under the caption *The Merger Material U.S. Federal Income Tax Consequences of the Merger* constitute the opinions of Pillsbury and Cooley, respectively. In rendering their opinions, counsel assume that the statements and facts concerning the Merger set forth in this proxy statement/prospectus/information statement and in the Merger Agreement, are true and accurate in all respects, and that the Merger will be completed in accordance with this proxy statement/prospectus/information statement and the Merger Agreement. Counsels opinions also assume the truth and accuracy of certain representations and covenants as to factual matters made by Signal, Miragen and Merger Sub in tax representation letters provided to counsel. In addition, counsel base their tax opinions on the law in effect on the date of the opinions and assume that there will be no change in applicable law between such date and the time of the Merger. If any of these assumptions is inaccurate, the tax consequences of the Merger could differ from those described in this proxy statement/prospectus/information statement.

No ruling from the IRS has been or will be requested with respect to the tax consequences of the Merger. Opinions of counsel do not bind the courts or the IRS, nor will they preclude the IRS from adopting a position contrary to those expressed in the opinions. Subject to the qualifications and assumptions described in this proxy statement/prospectus/information statement, the Merger will be treated for U.S. federal income tax purposes as a reorganization within the meaning of Section 368(a) of the Code. Accordingly, the tax consequences to U.S. Holders of Miragen common stock will be as follows:

- a U.S. Holder will not recognize gain or loss upon the exchange of Miragen common stock for Signal common stock pursuant to the Merger, except to the extent of cash received in lieu of a fractional share of Signal common stock as described below;

- a U.S. Holder who receives cash in lieu of a fractional share of Signal common stock in the Merger will recognize capital gain or loss in an amount equal to the difference between the amount of cash received instead of a fractional share and the stockholder s tax basis allocable to such fractional share;

- a U.S. Holder s aggregate tax basis for the shares of Signal common stock received in the Merger (including any fractional share interest for which cash is received) will equal the stockholder s aggregate tax basis in the shares of Miragen common stock surrendered in the Merger; and

- the holding period of the shares of Signal common stock received by a U.S. Holder in the Merger will include the holding period of the shares of Miragen common stock surrendered in exchange therefor.

Gain or loss recognized by a U.S. Holder who receives cash in lieu of a fractional share of Signal common stock will constitute capital gain or loss and any such gain or loss will constitute long-term capital gain or loss if the U.S. Holder s holding period in the Miragen common stock surrendered in the Merger is more than one year as of the effective date of the Merger. Under current law, long-term capital gains of non-corporate taxpayers are taxed at a reduced U.S. federal income tax rate. Under current law, the deductibility of capital losses is subject to limitations. In addition, for purposes of the above discussion of the bases and holding periods for shares of Miragen common stock and Signal common stock, U.S. Holders who acquired different blocks of Miragen common stock at different times for different prices must calculate their gains and losses and holding periods separately for each identifiable block of such stock exchanged in the Merger.

As provided in Treasury Regulations Section 1.368-3(d), each U.S. Holder who receives shares of Signal common stock in the Merger is required to retain permanent records pertaining to the Merger, and make such records available to any authorized IRS officers and employees. Such records should specifically include information regarding the amount, basis, and fair market value of all transferred property, and relevant facts regarding any liabilities assumed or extinguished as part of such reorganization. Additionally, U.S. Holders who owned immediately before the Merger at least one percent (by vote or value) of the total outstanding stock of Miragen are required to attach a statement to their tax returns for the year in which the Merger is consummated that contains the information listed in Treasury Regulation Section 1.368-3(b). Such statement must include the

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U.S. Holder s tax basis in such holder s Miragen common stock surrendered in the Merger, the fair market value of such stock, the date of the Merger and the name and employer identification number of each of Miragen and Signal.

If the Merger fails to qualify as a reorganization within the meaning of Section 368(a) of the Code, then a U.S. Holder would recognize gain or loss upon the exchange of Miragen common stock for Signal common stock equal to the difference between the fair market value, at the time of the Merger, of the Signal common stock received in the Merger (including any cash received in lieu of a fractional share of Signal common stock) and such U.S. Holder s tax basis in the Miragen common stock surrendered in the Merger. Such gain or loss would be long-term capital gain or loss if the Miragen common stock was held for more than one year at the time of the Merger. In such event, the aggregate tax basis of Signal common stock received in the Merger would equal its fair market value at the time of the closing of the Merger, and the holding period of such Signal common stock would commence the day after the closing of the Merger.

Information Reporting and Backup Withholding

A U.S. Holder of Miragen common stock may be subject to information reporting and backup withholding for U.S. federal income tax purposes on cash paid in lieu of fractional shares in connection with the Merger. The current backup withholding rate is 28 percent. Backup withholding will not apply, however, to a holder who (i) furnishes a correct taxpayer identification number and certifies the holder is not subject to backup withholding on IRS Form W-9 or a substantially similar form, (ii) provides a certification of foreign status on an appropriate IRS Form W-8 or successor form or (iii) certifies the holder is otherwise exempt from backup withholding. U.S. Holders of Miragen common stock should consult their tax advisors regarding their qualification for an exemption from backup withholding and the procedures for obtaining such an exemption. If a U.S. Holder does not provide a correct taxpayer identification number on IRS Form W-9 or other proper certification, the stockholder may be subject to penalties imposed by the IRS. Any amounts withheld under the backup withholding rules may be refunded or allowed as a credit against a U.S. Holder of Miragen common stock s federal income tax liability, if any, provided the required information is timely furnished to the IRS. In the event of backup withholding see your tax advisor to determine if you are entitled to any tax credit, tax refund or other tax benefit as a result of such backup withholding.

U.S. HOLDERS OF MIRAGEN COMMON STOCK SHOULD CONSULT THEIR TAX ADVISORS AS TO THE SPECIFIC TAX CONSEQUENCES TO THEM OF THE MERGER, INCLUDING THE APPLICABLE U.S. FEDERAL, STATE, LOCAL AND NON-U.S. INCOME AND OTHER TAX CONSEQUENCES, AND ANY TAX REPORTING REQUIREMENTS OF THE MERGER AND RELATED TRANSACTIONS IN LIGHT OF THEIR PARTICULAR CIRCUMSTANCES.

Anticipated Accounting Treatment

The Merger will be treated by Signal as a reverse merger under the acquisition method of accounting in accordance with U.S. GAAP. For accounting purposes, Miragen is considered to be acquiring Signal in this transaction. Management of Signal and Miragen have made a preliminary estimate of the purchase price calculated as described in Note 2 to the unaudited pro forma condensed combined financial statements. The net tangible assets acquired and liabilities assumed in connection with the transaction are recorded at their estimated acquisition date fair values. The acquisition method of accounting is dependent upon certain valuations and other studies that have yet to commence or progress to a stage where there is sufficient information for a definitive measurement. A final determination of these estimated fair values, which cannot be made prior to the completion of the transaction, will be based on the actual net tangible assets of Signal that exist as of the date of completion of the transaction.

NASDAQ Stock Market Listing

Signal common stock currently is listed on The NASDAQ Capital Market under the symbol SGNL. Signal has agreed to use commercially reasonable efforts to (i) maintain its existing listing on The NASDAQ Capital Market

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and to obtain approval of the listing of the combined company on The NASDAQ Capital Market, (ii) prepare and submit to The NASDAQ Capital Market a notification form for the listing of the shares of Signal common stock to be issued to Miragen stockholders pursuant to the Merger and the reverse split, (iii) cause such shares to be approved for listing and (iv) the extent required by NASDAQ Marketplace Rule 5110, file an initial listing application for the combined company on The NASDAQ Capital Market and to cause such listing application to be approved for listing. In addition, under the Merger Agreement, each of Miragen s and Signal s obligation to complete the Merger is subject to the satisfaction or waiver by each of the parties, at or prior to the Merger, of various conditions, including that the existing shares of Signal common stock must have been continually listed on The NASDAQ Capital Market, Signal must have caused the shares of Signal common stock to be issued in the Merger to be approved for listing on The NASDAQ Capital Market as of the effective time of the Merger and, to the extent required by NASDAQ Marketplace Rule 5110, the initial listing application for the combined company must be approved for listing. If such application is accepted, Signal anticipates that its common stock will be listed on The NASDAQ Capital Market following the closing of the Merger under the trading symbol MGEN.

Appraisal Rights and Dissenters Rights

Delaware Law

If the Merger is completed, Miragen stockholders who do not deliver a written consent approving the Merger are entitled to appraisal rights under Section 262 of the DGCL, or Section 262, provided that they comply with the conditions established by Section 262. Holders of Signal common stock are not entitled to appraisal rights under Delaware law in connection with the Merger.

The discussion below is not a complete summary regarding a Miragen stockholder s appraisal rights under Delaware law and is qualified in its entirety by reference to the text of the relevant provisions of Delaware law, which are attached to this proxy statement/prospectus/information statement as *Annex J*. Stockholders intending to exercise appraisal rights should carefully review *Annex J*. Failure to follow precisely any of the statutory procedures set forth in *Annex J* may result in a termination or waiver of these rights. This summary does not constitute legal or other advice, nor does it constitute a recommendation that Miragen stockholders exercise their appraisal rights under Delaware law.

Under Section 262, where a Merger is adopted by stockholders by written consent in lieu of a meeting of stockholders pursuant to Section 228 of the DGCL, either the constituent corporation before the effective date of the Merger or the surviving corporation, within 10 days after the effective date of the Merger, must notify each stockholder of the constituent corporation entitled to appraisal rights of the approval of the Merger, the effective date of the Merger and that appraisal rights are available.

If the Merger is completed, within 10 days after the effective date of the Merger Miragen will notify its stockholders that the Merger has been approved, the effective date of the Merger and that appraisal rights are available to any stockholder who has not approved the Merger. Holders of shares of Miragen capital stock who desire to exercise their appraisal rights must deliver a written demand for appraisal to Miragen within 20 days after the date of mailing of that notice, and that stockholder must not have delivered a written consent approving the Merger. A demand for appraisal must reasonably inform Miragen of the identity of the stockholder and that such stockholder intends thereby to demand appraisal of the shares of Miragen capital stock held by such stockholder. Failure to deliver a written consent approving the Merger will not in and of itself constitute a written demand for appraisal satisfying the requirements of Section 262. All demands for appraisal should be addressed to Miragen Therapeutics, Inc., 6200 Lookout Road, Boulder, CO 80301, Attention: Corporate Secretary, and should be executed by, or on behalf of, the record holder of shares of Miragen capital stock. ALL DEMANDS MUST BE RECEIVED BY MIRAGEN WITHIN 20 DAYS

AFTER THE DATE MIRAGEN MAILS A NOTICE TO ITS STOCKHOLDERS NOTIFYING THEM THAT THE MERGER HAS BEEN APPROVED, THE EFFECTIVE DATE OF THE MERGER AND THAT APPRAISAL RIGHTS ARE AVAILABLE TO ANY STOCKHOLDER WHO HAS NOT APPROVED THE MERGER.

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If you fail to deliver a written demand for appraisal within the time period specified above, you will be entitled to receive the Merger consideration for your shares of Miragen capital stock as provided for in the Merger Agreement, but you will have no appraisal rights with respect to your shares of Miragen capital stock.

To be effective, a demand for appraisal by a holder of shares of Miragen capital stock must be made by, or in the name of, the registered stockholder, fully and correctly, as the stockholder s name appears on the stockholder s stock certificate(s). Beneficial owners who do not also hold the shares of record may not directly make appraisal demands to Miragen. The beneficial owner must, in these cases, have the registered owner, such as a broker, bank or other custodian, submit the required demand in respect of those shares. If shares are owned of record in a fiduciary capacity, such as by a trustee, guardian or custodian, execution of a demand for appraisal should be made by or for the fiduciary; and if the shares are owned of record by more than one person, as in a joint tenancy or tenancy in common, the demand should be executed by or for all joint owners. An authorized agent, including an authorized agent for two or more joint owners, may execute the demand for appraisal for a stockholder of record; however, the agent must identify the record owner or owners and expressly disclose the fact that, in executing the demand, he or she is acting as agent for the record owner. A record owner, such as a broker, who holds shares as a custodian for others, may exercise the record owner s right of appraisal with respect to the shares held for one or more beneficial owners, while not exercising this right for other beneficial owners. In that case, the written demand should state the number of shares as to which appraisal is sought. Where no number of shares is expressly mentioned, the demand will be presumed to cover all shares held in the name of the record owner. In addition, the stockholder must continuously hold the shares of record from the date of making the demand through the effective time of the Merger.

If you hold your shares of Miragen capital stock in a brokerage account or in other custodian form and you wish to exercise appraisal rights, you should consult with your bank, broker or other custodian to determine the appropriate procedures for the making of a demand for appraisal by the custodian.

At any time within 60 days after the effective time of the Merger, any stockholder who has demanded an appraisal, but has neither commenced an appraisal proceeding or joined an appraisal proceeding as a named party, has the right to withdraw such stockholder s demand and accept the terms of the Merger by delivering a written withdrawal to Miragen. If, following a demand for appraisal, you have withdrawn your demand for appraisal in accordance with Section 262, you will have the right to receive the Merger consideration for your shares of Miragen capital stock.

Within 120 days after the effective date of the Merger, any stockholder who has delivered a demand for appraisal in accordance with Section 262 will, upon written request to the surviving corporation, be entitled to receive a written statement setting forth the aggregate number of shares not voted in favor of the Merger Agreement and with respect to which demands for appraisal rights have been received and the aggregate number of holders of these shares. This written statement will be mailed to the requesting stockholder within 10 days after the stockholder s written request is received by the surviving corporation or within 10 days after expiration of the period for delivery of demands for appraisal, whichever is later. Within 120 days after the effective date of the Merger, either the surviving corporation or any stockholder who has delivered a demand for appraisal in accordance with Section 262 may file a petition in the Delaware Court of Chancery demanding a determination of the fair value of the shares held by all such stockholders. Upon the filing of the petition by a stockholder, service of a copy of the petition must be made upon the surviving corporation. The surviving corporation has no obligation to file a petition in the Delaware Court of Chancery in the event there are dissenting stockholders, and Miragen, which is expected to be the surviving corporation, has no present intent to file a petition in the Delaware Court of Chancery. Accordingly, the failure of a stockholder to file a petition within the period specified could nullify the stockholder s previously written demand for appraisal.

If a petition for appraisal is duly filed by a stockholder and a copy of the petition is delivered to the surviving corporation, the surviving corporation will then be obligated, within 20 days after receiving service of a copy of the

petition, to provide the Delaware Court of Chancery with a duly verified list containing the names and

addresses of all stockholders who have demanded an appraisal of their shares and with whom agreements as to the value of their shares have not been reached by the surviving corporation. After notice to dissenting stockholders who demanded appraisal of their shares, the Delaware Court of Chancery is empowered to conduct a hearing upon the petition, and to determine those stockholders who have complied with Section 262 and who have become entitled to the appraisal rights provided thereby. The Delaware Court of Chancery may require the stockholders who have demanded appraisal for their shares to submit their stock certificates to the Register in Chancery for notation thereon of the pendency of the appraisal proceedings; and if any stockholder fails to comply with that direction, the Delaware Court of Chancery may dismiss the proceedings as to that stockholder.

After determination of the stockholders entitled to appraisal of their shares, the Delaware Court of Chancery will appraise the fair value of the shares owned by those stockholders. This value will be exclusive of any element of value arising from the accomplishment or expectation of the Merger, but may include a fair rate of interest, if any, upon the amount determined to be the fair value. When the value is determined, the Delaware Court of Chancery will direct the payment of the value, with interest thereon accrued during the pendency of the proceeding, if the Delaware Court of Chancery so determines, to the stockholders entitled to receive the same, upon surrender by the holders of the certificates representing those shares. At any time before the entry of judgment in the proceedings, the surviving corporation may pay to each stockholder entitled to appraisal an amount in cash, in which case interest shall accrue thereafter only upon the sum of (i) the difference, if any, between the amount so paid and the fair value of the shares subject to appraisal as determined by the Delaware Court of Chancery and (ii) interest theretofore accrued, unless paid at that time.

In determining fair value, and, if applicable, a fair rate of interest, the Delaware Court of Chancery is required to take into account all relevant factors. In *Weinberger v. UOP, Inc.*, the Delaware Supreme Court discussed the factors that could be considered in determining fair value in an appraisal proceeding, stating that proof of value by any techniques or methods which are generally considered acceptable in the financial community and otherwise admissible in court should be considered, and that fair price obviously requires consideration of all relevant factors involving the value of a company.

Section 262 provides that fair value is to be exclusive of any element of value arising from the accomplishment or expectation of the Merger. In *Cede & Co. v. Technicolor, Inc.*, the Delaware Supreme Court stated that this exclusion is a narrow exclusion [that] does not encompass known elements of value, but which rather applies only to the speculative elements of value arising from such accomplishment or expectation. In *Weinberger*, the Delaware Supreme Court construed Section 262 to mean that elements of future value, including the nature of the enterprise, which are known or susceptible of proof as of the date of the Merger and not the product of speculation, may be considered.

You should be aware that the fair value of your shares as determined under Section 262 could be more than, the same as, or less than the value that you are entitled to receive under the terms of the Merger Agreement.

Costs of the appraisal proceeding may be imposed upon the surviving corporation and the stockholders participating in the appraisal proceeding by the Delaware Court of Chancery as the Court deems equitable in the circumstances. Upon the application of a stockholder, the Delaware Court of Chancery may order all or a portion of the expenses incurred by any stockholder in connection with the appraisal proceeding, including, without limitation, reasonable attorneys fees and the fees and expenses of experts, to be charged pro rata against the value of all shares entitled to appraisal. In the absence of such a determination of assessment, each party bears its own expenses. Any stockholder who had demanded appraisal rights will not, after the effective time of the Merger, be entitled to vote shares subject to that demand for any purpose or to receive payments of dividends or any other distribution with respect to those shares, other than with respect to payment as of a record date prior to the effective time; however, if no petition for appraisal

is filed within 120 days after the effective time of the Merger, or if the stockholder delivers a written withdrawal of his or her demand for appraisal and an acceptance of the terms of the Merger within 60 days after the effective time of the Merger, then the right of that stockholder to appraisal will cease and that stockholder will be entitled to receive the Merger consideration for shares of his

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or her Miragen capital stock pursuant to the Merger Agreement. Any withdrawal of a demand for appraisal made more than 60 days after the effective time of the Merger may only be made with the written approval of the surviving corporation. No appraisal proceeding in the Delaware Court of Chancery will be dismissed as to any stockholder without the approval of the court.

Failure to follow the steps required by Section 262 for perfecting appraisal rights may result in the loss of appraisal rights. In view of the complexity of Section 262, stockholders who may wish to dissent from the Merger and pursue appraisal rights should consult their legal advisors.

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THE MERGER AGREEMENT

The following is a summary of the material terms of the Merger Agreement. A copy of the Merger Agreement is attached as Annex A to this proxy statement/prospectus/information statement and is incorporated by reference into this proxy statement/prospectus/information statement. The Merger Agreement has been attached to this proxy statement/prospectus/information statement to provide you with information regarding its terms. It is not intended to provide any other factual information about Signal, Miragen or Merger Sub. The following description does not purport to be complete and is qualified in its entirety by reference to the Merger Agreement. You should refer to the full text of the Merger Agreement for details of the Merger and the terms and conditions of the Merger Agreement.

The Merger Agreement contains representations and warranties that Signal and Merger Sub, on the one hand, and Miragen, on the other hand, have made to one another as of specific dates. These representations and warranties have been made for the benefit of the other parties to the Merger Agreement and may be intended not as statements of fact but rather as a way of allocating the risk to one of the parties if those statements prove to be incorrect. In addition, the assertions embodied in the representations and warranties are qualified by information in confidential disclosure schedules exchanged by the parties in connection with signing the Merger Agreement. While Signal and Miragen do not believe that these disclosure schedules contain information required to be publicly disclosed under the applicable securities laws, other than information that has already been so disclosed, the disclosure schedules do contain information that modifies, qualifies and creates exceptions to the representations and warranties set forth in the attached Merger Agreement. Accordingly, you should not rely on the representations and warranties as current characterizations of factual information about Signal or Miragen, because they were made as of specific dates, may be intended merely as a risk allocation mechanism between Signal and Merger Sub, and Miragen and are modified by the disclosure schedules.

Structure

Under the Merger Agreement, Merger Sub will merge with and into Miragen, with Miragen surviving as a wholly-owned subsidiary of Signal.

Completion and Effectiveness of the Merger

The Merger will be completed as promptly as practicable after all of the conditions to completion of the Merger are satisfied or waived, including the approval of the stockholders of Signal and Miragen. Signal and Miragen are working to complete the Merger as quickly as practicable. However, Signal and Miragen cannot predict the exact timing of the completion of the Merger because it is subject to various conditions.

Merger Consideration and Exchange Ratio

Immediately prior to the effective time of the Merger, each outstanding shares of preferred stock of Miragen will be converted into common stock. At the effective time of the Merger,

- each outstanding share of common stock of Miragen will be converted into the right to receive that number of shares of Signal common stock as determined pursuant to the Exchange Ratio described in more detail below;

each outstanding option to purchase shares of Miragen common stock will be assumed by Signal and will be converted into an option to purchase shares of Signal common stock; and

each outstanding warrant to purchase shares of Miragen capital stock will be assumed by Signal and will be converted into a warrant to purchase shares of Signal common stock.

No fractional shares of Signal common stock will be issued in connection with the Merger. Instead, each Miragen stockholder who otherwise would be entitled to receive a fractional share of Signal common stock

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(after aggregating all fractional shares of Signal common stock issuable to such holder) will be entitled to receive an amount in cash representing such holder s proportionate interest, if any, in the proceeds from the sale of the aggregated fractional shares by the exchange agent (reduced by any fees of the exchange agent attributable to such sale) at the then prevailing prices on the NASDAQ Capital Market.

The Exchange Ratio is calculated using a formula intended to allocate existing Miragen securityholders (on a fully-diluted basis), a percentage of the combined company. Based on Miragen s and Signal s capitalization as of December 31, 2016, the Exchange Ratio is currently estimated to be (i) approximately 0.6995 pre-split shares of Signal common stock, subject to adjustment to account for the effect of a reverse stock split of Signal common stock, within a range of one new share for every one to 15 shares outstanding, to be implemented prior to the consummation of the Merger as discussed in this proxy statement/prospectus/information statement or (ii), post-split, between approximately 0.6995 and 0.0466 shares of Signal common stock. These estimates are subject to adjustment prior to closing of the Merger, including (i) adjustments to account for the issuance of any additional shares of Miragen or Signal common stock, as applicable, prior to the consummation of the Merger, provided that, the issuance of Miragen common stock in the concurrent financing will not impact the Exchange Ratio, or (ii) an upward adjustment to the extent that Signal s net cash at the effective time of the Merger is less than negative $100,000 (and as a result, Signal securityholders could own less, and Miragen securityholders could own more, of the combined company).

Based on the estimates set forth above, following the completion of the Merger, Miragen securityholders would own approximately 96% of the fully-diluted common stock of the combined company and Signal securityholders would own approximately 4% of the fully-diluted common stock of the combined company, each assuming that Miragen closes its concurrent financing immediately prior to the effective time of the Merger. If the concurrent financing does not close, then Miragen securityholders would own approximately 94% of the fully-diluted common stock of the combined company and Signal securityholders would own approximately 6% of the fully-diluted common stock of the combined company.

The Exchange Ratio formula is the quotient obtained by dividing the number of Miragen merger shares (defined below) by the Miragen fully-diluted outstanding shares (defined below), where:

Miragen merger shares is the product determined by *multiplying* (i) the post-closing Signal shares *by* (ii) the Miragen allocation percentage.

Miragen fully-diluted outstanding shares is the total number of shares of Miragen common stock outstanding immediately prior to the effective time of the Merger on a fully-diluted and an as-converted to common stock basis, assuming the exercise of each outstanding Miragen option and Miragen warrant to purchase Miragen capital stock and the effectiveness of the conversion of all of Miragen s outstanding preferred stock into Miragen common stock; provided, however, that all shares of Miragen common stock issued in its concurrent financing will be excluded from such amount.

Post-closing Signal shares is the quotient determined by *dividing (i) the Signal fully-diluted outstanding shares by* (ii) the Signal allocation percentage.

Signal fully-diluted outstanding shares is the total number of shares of Signal common stock outstanding immediately prior to the effective time of the Merger on a fully-diluted and an as-converted to common stock basis, assuming (i) the exercise of each outstanding Signal option to purchase Signal common stock (to the extent such option will not be cancelled pursuant to the Merger Agreement), (ii) the settlement in shares of Signal common stock of each outstanding Signal restricted stock unit (to the extent such restricted stock until will not be cancelled pursuant to the Merger Agreement), (iii) the exercise of each outstanding Signal warrant to purchase common stock, and (iv) the conversion of the indebtedness into Signal common stock in accordance with the terms and conditions of the Note Amendment.

Miragen allocation percentage is 1.00 ***minus*** the Signal allocation percentage.

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Signal allocation percentage is 0.06; *provided, however, solely* to the extent that the net cash determined pursuant to the Merger Agreement is less than negative $100,000, then 0.06 shall be reduced by 0.00000002 for each $1.00 that the Net Cash as so determined is less than negative $100,000 (for example, the Signal allocation percentage would be 0.055 if Signal s net cash is negative $350,000).

Determination of Signal s Net Cash

For purposes of determining the Exchange Ratio and determining whether Signal has satisfied the condition to closing, Signal must have at least negative $300,000 in net cash as of the closing date (as calculated pursuant to the terms of the Merger Agreement). Signal s net cash will be calculated shortly before the closing date of the Merger. The closing of the Merger could be delayed if Miragen and Signal are not able to agree upon the amount of Signal s net cash as of Signal s cash determination date.

Under the Merger Agreement, Signal s net cash is defined as (i) the sum of Signal s cash and cash equivalents, marketable securities, accounts, interest and other receivables (to the extent determined to be collectible), and deposits (to the extent refundable to Signal), in each case as of the anticipated closing date, determined in a manner consistent with the manner in which such items were historically determined and in accordance with Signal s audited financial statements and Signal s unaudited interim balance sheet, *minus* (ii) the sum of Signal s accounts payable and accrued expenses (without duplication of any expenses accounted for below), in each case as of such date and determined in a manner consistent with the manner in which such items were historically determined and in accordance with Signal s audited financial statements and Signal s unaudited interim balance sheet, *minus* (iii) the cash cost of any unpaid change of control payments or severance, termination or similar payments that are or become due to any current or former employee, director or independent contractor of Signal, or any other third party *minus* (iv) the cash cost of any accrued and unpaid retention payments or other bonuses due to any current or former employee, director or independent contractor of Signal as of the closing date, *minus* (v) the cash cost of any other payments to terminated Signal employees not set forth in clauses (iii) or (iv), *minus* (vi) all payroll, employment or other withholding taxes incurred by Signal and any Signal employee (to the extent paid or to be paid by Signal on the behalf of such employee) in connection with any payment amounts set forth in clauses (iii), (iv) or (v) and the exercise of any Signal option or settlement of any Signal restricted stock unit on or prior to the effective time, *minus* (vii) any remaining unpaid fees and expenses (including any attorney s, accountant s, financial advisor s or finder s fees) as of such date for which Signal is liable incurred by Signal in connection with the Merger Agreement and the Merger and other transactions contemplated by the Merger Agreement or otherwise, *minus* (viii) any bona fide current liabilities payable in cash, in each case to the extent not cancelled at or prior to the anticipated closing date, *minus* (ix) any fees and expenses payable by Signal pursuant to the Merger Agreement, *minus* (x) any unpaid amounts payable by Signal in satisfaction of its obligations under the Merger Agreement for the period after the closing (including any expenses incurred in connection with the tail policy), *minus* (xi) the cash cost of any unpaid retention payment amounts due under any insurance policy with respect to any legal proceeding against Signal or Merger Sub, *minus* (xii) the cash cost of repurchasing any shares of Signal common stock to the extent Signal has agreed to purchase such shares and the purchase price for such shares has not been fully paid by Signal as of the determination date, *plus* or *minus* (as applicable) (xiii) the net amount of any transaction expense reimbursements owed to, or transaction expense payment owed by, Signal pursuant to the Merger Agreement, *plus* (xiv) the amount of any payments due to Signal within 30 days of the closing date pursuant to the sale or other disposition of all or a portion of Signal s lab business, *plus* (xv) any amounts paid or payable by Signal for activities requested by Miragen in respect of the audit of Signal s financial statements at and for the year ended December 31, 2016, as well as for the preparation of Signal s Annual Report on Form 10-K for 2016.

Signal s net cash balance at the determination date is subject to numerous factors, many of which are outside of Signal s control. If Signal s net cash at the closing date is less than negative $300,000, based on the manner of

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calculating net cash pursuant to the Merger Agreement, Signal would be unable to satisfy a closing condition for the Merger, and Miragen could elect to waive the condition or not affect the Merger. Furthermore, the Exchange Ratio at the closing will be subject to an upward adjustment to the extent that Signal s net cash at the effective time of the Merger is less than negative $100,000 (and as a result, Signal securityholders could own less, and Miragen securityholders could own more, of the combined company), as described under *The Merger Agreement Merger Consideration and Exchange Ratio*.

Signal Common Stock

Prior to giving effect to the reverse stock split, each share of Signal common stock issued and outstanding at the time of the Merger will remain issued and outstanding and those shares will be unaffected by the Merger. After giving effect to the reverse stock split, each one to 15 shares (or any number in between) of Signal common stock issued and outstanding would be combined and reclassified into one share of Signal common stock. Signal stock options and restricted stock units that remain unexercised or unsettled, as applicable, as of the effective time will be cancelled and terminated. Immediately after the Merger, Signal securityholders will own approximately 4% of the fully-diluted common stock of the combined company, assuming that Miragen closes its concurrent financing immediately prior to the effective time of the Merger. If the concurrent financing does not close, then Signal s securityholders would own the approximately 6% of the fully-diluted common stock of the combined company.

Procedures for Exchanging Miragen Stock Certificates

Promptly after the effective time of the Merger, VStock Transfer LLC, as the exchange agent for the Merger, will establish an exchange fund to hold the shares of Signal common stock to be issued to Miragen stockholders in connection with the Merger.

As promptly as practicable following the completion of the Merger, the exchange agent will mail to each holder of record of Miragen capital stock a letter of transmittal and instructions for surrendering the record holder s stock certificates in exchange for the shares of Signal common stock. Upon proper surrender of Miragen stock certificates together with a properly completed and duly executed letter of transmittal in accordance with the exchange agent s instructions, the holder of such Miragen stock certificates will be entitled to receive shares representing the number of whole shares of Signal common stock issuable to such holder pursuant to the Merger and cash in lieu of any fractional share of Signal common stock issuable to such holder. The surrendered certificates representing Miragen capital stock will be cancelled.

After the effective time of the Merger, each certificate representing shares of Miragen capital stock that has not been surrendered will represent only the right to receive shares of Signal common stock issuable pursuant to the Merger and cash in lieu of any fractional share of Signal common stock to which the holder of any such certificate is entitled. No interest will be paid or accrued on any cash in lieu of fractional shares payable to holders of Miragen stock certificates.

Any holder or former holder of Miragen capital stock may be subject to withholding under the Code, or under another provision of state, local or foreign tax law. To the extent such amounts are withheld and paid to the appropriate governmental entity, they will be treated as having been paid to the person to whom such amounts would otherwise have been paid.

HOLDERS OF MIRAGEN CAPITAL STOCK SHOULD NOT SEND IN THEIR MIRAGEN STOCK CERTIFICATES UNTIL THEY RECEIVE A LETTER OF TRANSMITTAL FROM THE EXCHANGE AGENT WITH INSTRUCTIONS FOR THE SURRENDER OF MIRAGEN STOCK CERTIFICATES.

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Fractional Shares

No fractional shares of Signal common stock will be issuable pursuant to the Merger to Miragen stockholders. Instead, each Miragen stockholder who would otherwise be entitled to receive a fraction of a share of Signal common stock, after aggregating all fractional shares of Signal common stock issuable to such stockholder, will be entitled to receive a cash payment in lieu of such fractional shares representing such holder s proportionate interest, if any, in the proceeds from the sale by the exchange agent (reduced by any fees attributable to such sale) in one or more transactions of shares of Signal common stock equal to the excess of (i) the aggregate number of shares of Signal common stock issuable in exchange for all outstanding shares of Miragen capital stock over (ii) the aggregate number of whole shares of Signal common stock to be distributed to holders of Miragen stock certificates.

Representations and Warranties

The Merger Agreement contains customary representations and warranties made by Signal, Merger Sub and Miragen relating to their respective businesses, as well as other facts pertinent to the Merger. These representations and warranties are subject to materiality, knowledge and other similar qualifications in many respects and expire at the effective time of the Merger or termination of the Merger Agreement, as further described below. The representations and warranties of each of Signal, Merger Sub and Miragen have been made solely for the benefit of the other parties and those representations and warranties should not be relied on by any other person. In addition, those representations and warranties may be intended not as statements of actual fact, but rather as a way of allocating risk among the parties, may have been modified by the disclosure schedules delivered in connection with the Merger Agreement, are subject to the materiality standard described in the Merger Agreement, which may differ from what may be viewed as material by you, will not survive completion of the Merger and cannot be the basis for any claims under the Merger Agreement by the other parties after termination of the Merger Agreement, and were made only as of the date of the Merger Agreement or another date as is specified in the Merger Agreement.

Miragen made a number of representations and warranties to Signal and Merger Sub in the Merger Agreement, including representations and warranties relating to the following matters:

- subsidiaries; due organization; organizational documents;
- authority; vote required;
- non-contravention; consents;
- capitalization;
- financial statements;
- absence of changes;

title to assets;

real property; leaseholds;

intellectual property;

material contracts;

undisclosed liabilities;

compliance; permits; restrictions;

tax matters;

employee and labor matters; benefit plans;

environmental matters;

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insurance;

legal proceedings; orders;

inapplicability of anti-takeover statutes;

no financial advisor;

subscription agreement;

disclosure; and

exclusivity of representations; reliance.

Significant portions of Miragen s representations and warranties are qualified as to materiality or material adverse effect. Under the Merger Agreement, a material adverse effect with respect to Miragen means any effect, change, event, circumstance or development that has occurred prior to the date of determination of the occurrence of such material adverse effect, that is or would reasonably be expected to be materially adverse to or has or would reasonably be expected to have or result in a material adverse or effect on (i) the business, condition (financial or otherwise), capitalization, assets, operations or financial performance of Miragen and its subsidiaries, taken as a whole or (ii) the ability of Miragen to consummate the transactions contemplated by the Merger Agreement or perform any of its covenants or obligations under the Merger Agreement in all material respects, except that none of the following, as they apply to Miragen and its subsidiaries, will be taken into account in determining whether there has been a material adverse effect:

any rejection by a governmental body of a registration or filing by Miragen relating to Miragen s intellectual property rights;

any change in the cash position of Miragen that results from operations in the ordinary course of business;

conditions generally affecting the industries in which Miragen and its subsidiaries participate or the U.S. or global economy or capital markets as a whole, to the extent that such conditions do not have a disproportionate impact on Miragen and its subsidiaries, taken as a whole;

any failure by Miragen or any of its subsidiaries to meet internal projections or forecasts on or after the date of the Merger Agreement, provided that any such effect, change, event, circumstance or development causing or contributing to any such failure to meet projections or forecasts may constitute a material adverse effect of Miragen and may be taken into account in determining whether a material adverse effect has

occurred;

the execution, delivery, announcement or performance of obligations under the Merger Agreement or the announcement, pendency or anticipated consummation of the Merger or Miragen s concurrent financing;

the failure to close Miragen s concurrent financing;

any natural disaster or any acts of terrorism, sabotage, military action or war or any escalation or worsening thereof; or

any changes after the date of the Merger Agreement in U.S. GAAP or applicable laws.

Signal and Merger Sub made a number of representations and warranties to Miragen in the Merger Agreement, including representations and warranties relating to the following subject matters:

subsidiaries; due organization; organizational documents;

authority; vote required;

non-contravention; consents;

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capitalization;

SEC filings; financial statements;

absence of changes;

title to assets;

real property; leaseholds;

intellectual property;

material contracts;

undisclosed liabilities;

compliance; permits; restrictions;

tax matters;

employee and labor matters; benefit plans;

environmental matters;

insurance;

legal proceedings; orders;

inapplicability of anti-takeover statutes;

no financial advisor;

disclosure;

bank accounts; deposits;

transactions with affiliates;

valid issuance;

code of ethics;

opinion of financial advisor;

shell company status; and

exclusivity of representations; reliance.

Similar to Miragen s representations and warranties, significant portions of Signal s representations and warranties are qualified as to materiality or material adverse effect. Under the Merger Agreement, a material adverse effect with respect to Signal means any effect, change, event, circumstance or development that has occurred prior to the date of determination of the occurrence of such material adverse effect, that is or would reasonably be expected to be materially adverse to or has or would reasonably be expected to have or result in a material adverse or effect on (i) the business, condition (financial or otherwise), capitalization, assets, operations or financial performance of Signal or (ii) the ability of Signal to consummate the transactions contemplated by the Merger Agreement or perform any of its covenants or obligations under the Merger Agreement in all material respects , except that none of the following, as they apply to Signal, will be taken into account in determining whether there has been a material adverse effect:

any rejection by a governmental body of a registration or filing by Signal relating to Signal s intellectual property rights;

any change in the cash position of Signal that results from operations in the ordinary course of business;

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conditions generally affecting the industries in which Signal and its subsidiaries participate or the U.S. or global economy or capital markets as a whole, to the extent that such conditions do not have a disproportionate impact on Signal;

any failure by Signal to meet internal projections or forecasts or third-party revenue or earnings predictions for any period ending (or for which revenues or earnings are released) on or after the date of the Merger Agreement or any change in the price or trading volume of Signal s common stock, provided that any such effect, change, event, circumstance or development causing or contributing to any such failure to meet projections or forecasts may constitute a material adverse effect of Miragen and may be taken into account in determining whether a material adverse effect has occurred;

the sale and/or winding down of Signal s lab business and other operations;

the execution, delivery, announcement or performance of obligations under the Merger Agreement or the announcement, pendency or anticipated consummation of the Merger or Miragen s concurrent financing;

any natural disaster or any acts of terrorism, sabotage, military action or war or any escalation or worsening thereof; or

any changes after the date of the Merger Agreement in U.S. GAAP or applicable laws.

Covenants; Conduct of Business Pending the Merger

During the period commencing on October 31, 2016 and ending at the earlier of the date of termination of the Merger Agreement and the effective time of the Merger, each party agreed that it will conduct its business in the ordinary course and in compliance with all applicable laws, rules, regulations, and certain material contracts and will provide the other party with prompt notice upon the occurrence of certain events or discovery of certain conditions, facts or circumstances.

Miragen also agreed that prior to the earlier of termination and the effective time of the Merger, subject to certain limited exceptions set forth in the Merger Agreement, without the consent of Signal, it would not and would not permit any of its subsidiaries to:

declare, accrue, set aside or pay any dividend or make any other distribution in respect of any shares of Miragen capital stock or repurchase, redeem or otherwise reacquire any shares of its capital stock or other securities except pursuant to Miragen contracts existing as of the date of the Merger Agreement;

sell, issue or grant, or authorize the issuance of any capital stock or other security (except in connection with the concurrent financing and for shares of Miragen common stock issued upon the valid exercise of Miragen options or Miragen warrants outstanding as of the date of the Merger Agreement), any option, warrant or right to purchase any capital stock or any other security (except for the grant of options to purchase up to an

aggregate 379,524 shares of Miragen common stock and except for any warrants issued to Silicon Valley Bank pursuant to the terms of Miragen s existing credit facility), any equity-based award or instrument convertible into or exchangeable for any capital stock or other security, or any debt securities or any rights to acquire any debt securities;

amend the certificate of incorporation, bylaws or other charter or organizational documents of Miragen (other than in connection with Miragen s concurrent financing), or effect or be a party to any Merger, consolidation, share exchange, business combination, recapitalization, reclassification of shares, stock split, reverse stock split or similar transaction;

form any subsidiary or acquire any equity interest or other interest in any other entity;

lend money to any person, incur or guarantee any indebtedness for borrowed money, other than in the ordinary course of business or under Miragen s existing credit facility with Silicon Valley Bank, guarantee any debt securities of others, or make any capital expenditure or commitment in excess of $250,000;

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enter into any contract with a labor union or collective bargaining agreement;

acquire any material asset nor sell, lease, or otherwise irrevocably dispose of any of its assets or properties, or grant any encumbrance with respect to such assets or properties, in each case, other than in the ordinary course of business;

make, change or revoke any material tax election, file any material amendment to any tax return, adopt or change any accounting method in respect of taxes, change any annual tax accounting period, enter into any tax allocation agreement, tax sharing agreement or tax indemnity agreement, other than commercial contracts entered into in the ordinary course of business with vendors, customers or landlords, enter into any closing agreement with respect to any tax, settle or compromise any claim, notice, audit report or assessment in respect of material taxes, apply for or enter into any ruling from any tax authority with respect to taxes, surrender any right to claim a material tax refund, or consent to any extension or waiver of the statute of limitations period applicable to any material tax claim or assessment; or

agree, resolve or commit to do any of the foregoing.

Signal also agreed that prior to the earlier of termination and the effective time of the Merger, subject to certain limited exceptions set forth in the Merger Agreement, without the consent of Miragen, it would not:

declare, accrue, set aside or pay any dividend or make any other distribution in respect of any shares of Signal capital stock or repurchase, redeem or otherwise reacquire any shares of its capital stock or other securities;

sell, issue or grant, or authorize the issuance of any capital stock or other security (except for shares of Signal common stock issued upon the settlement of Signal restricted stock units or upon the valid exercise of Signal options or Signal warrants outstanding as of the date of the Merger Agreement), any option, warrant or right to purchase any capital stock or any other security, any equity-based award or instrument convertible into or exchangeable for any capital stock or other security, or any debt securities or any rights to acquire any debt securities;

amend the certificate of incorporation, bylaws or other charter or organizational documents of Signal or Merger Sub, or effect or be a party to any merger, consolidation, share exchange, business combination, recapitalization, reclassification of shares, stock split, reverse stock split or similar transaction;

form any subsidiary or acquire any equity interest or other interest in any other entity;

lend money to any person, incur or guarantee any indebtedness for borrowed money, other than in the ordinary course of business, guarantee any debt securities of others, or make any capital expenditure or commitment;

adopt, establish or enter into any Signal employee plan, cause or permit any Signal employee plan to be amended other than as required by law, including in order to make amendments for the purposes of Section 409A of the Code, subject to prior review and approval (with such approval not to be unreasonably withheld, conditioned or delayed) by Miragen, hire any additional employees or independent contractors or enter into or amend the term of any employment or consulting agreement with any employee or independent contractor other than as reasonably necessary for the completion of the transactions contemplated by the Merger Agreement, enter into any contract with a labor union or collective bargaining agreement, pay any bonus or make any profit-sharing or similar payment to (other than in the ordinary course of business), or increase the amount of the wages, salary, commissions, fringe benefits or other compensation or remuneration payable to, any of its directors or employees, accelerate the vesting of or entitlement to any payment, award, compensation or benefit with respect to any current or former Signal employee, pay or increase the severance or change of control benefits offered to any Signal Associate, or provide or make any Tax-related gross-up payment,

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provided, that Signal may pay payments to certain terminated employees in connection with their termination of employment or service;

enter into any material transaction outside the ordinary course of business;

acquire any material asset nor sell, lease, or otherwise irrevocably dispose of any of its assets or properties, or grant any encumbrance with respect to such assets or properties, other than in the ordinary course of business;

make, change or revoke any material tax election, file any material amendment to any tax return, adopt or change any accounting method in respect of taxes, change any annual tax accounting period, enter into any tax allocation agreement, tax sharing agreement or tax indemnity agreement, other than commercial contracts entered into in the ordinary course of business with vendors, customers or landlords, enter into any closing agreement with respect to any tax, settle or compromise any claim, notice, audit report or assessment in respect of material taxes, apply for or enter into any ruling from any tax authority with respect to taxes, surrender any right to claim a material tax refund, or consent to any extension or waiver of the statute of limitations period applicable to any material tax claim or assessment;

enter into, amend or terminate any Signal contract that, if effective as of the date hereof, would constitute a Signal material contract;

initiate or settle any legal proceeding;

after the net cash calculation is finalized pursuant to the Merger Agreement, incur any liabilities or otherwise take any actions other than in the ordinary course of business so as to cause the final net cash calculation to differ materially from actual net cash as of the closing; or

agree, resolve or commit to do any of the foregoing.

Non-Solicitation

The Merger Agreement contains provisions prohibiting Signal and Miragen from seeking a competing transaction, subject to specified exceptions described below. Under these non-solicitation provisions, each of Signal and Miragen has agreed that neither it nor its subsidiaries, nor any of its officers, directors, employees, representatives, affiliates, advisors or agents shall directly or indirectly: (i) solicit, initiate, respond to or take any action to facilitate or encourage any inquiries or the communication, making, submission or announcement of any competing proposal or take any action that could reasonably be expected to lead to a competing proposal; (ii) enter into or participate in any discussions or negotiations with any person with respect to any competing proposal; (iii) furnish any information regarding such party to any person in connection with, in response to, relating to or for the purpose of assisting with or facilitating a competing proposal; (iv) approve, endorse or recommend any competing proposal (subject to the terms and conditions of the Merger Agreement); (v) execute or enter into any letter of intent or similar document or any contract contemplating or otherwise relating to any competing proposal; or (vi) grant any waiver or release under any

confidentiality, standstill or similar agreement (other than to the other party).

However, prior to the approval of the proposals relating to the Merger set forth in this proxy statement/prospectus/information statement at the meeting of the stockholders of either Signal or by written consent of Miragen stockholders, as the case may be, (i) either Signal or Miragen may enter into discussions or negotiations with, any person that has made (and not withdrawn) a bona fide, unsolicited, competing proposal, which such party s board of directors determines in good faith, after consultation with its independent financial advisor, if any, and its outside legal counsel, constitutes, or would reasonably be expected to result in, a superior competing proposal, and (ii) thereafter furnish to such person non-public information regarding such party pursuant to an executed confidentiality agreement containing provisions (including nondisclosure provisions, use restrictions, non-solicitation provisions, no hire provisions and standstill provisions) at least as favorable to such party as

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those contained in the confidentiality agreement, but in each case of the foregoing clauses (i) and (ii), only if: (A) neither such party nor any representative of such party has breached its non-solicitation obligations; (B) the board of directors of such party determines in good faith based on the advice of outside legal counsel, that the failure to take such action would reasonably be expected to result in a breach of the fiduciary duties of the board of directors of such party under applicable laws; (C) at least five business days prior to furnishing any such non-public information to, or entering into discussions with, such person, such party gives the other party written notice of the identity of such person and of such party s intention to furnish nonpublic information to, or enter into discussions with, such person; and (D) at least five business days prior to furnishing any such non-public information to such person, such party furnishes such non-public information to Miragen or Signal, as applicable (to the extent such non-public information has not been previously furnished by such party to Miragen or Signal, as applicable). Without limiting the generality of the foregoing, each party has acknowledged and agreed that, in the event any representative of such party (whether or not such representative is purporting to act on behalf of such party) takes any action that, if taken by such party, would constitute a breach of the non-solicitation obligations of such party, the taking of such action by such representative shall be deemed to constitute a breach of these non-solicitation obligations of such party for purposes of the Merger Agreement.

Signal and Miragen will notify the other no later than 24 hours after receipt of any inquiries, discussions, negotiations, proposals or expressions of interest with respect to a competing proposal, and any such notice will be made orally and in writing and will indicate in reasonable detail the terms and conditions of such proposal, inquiry or contact, including price, and the identity of the offeror. Both Signal and Miragen will keep the other informed, on a current basis, of the status and material developments (including any changes to the terms) of such competing proposal.

A competing proposal is any of the following proposals, indications of interest or offers, other than transactions contemplated by the Merger Agreement:

- any merger, consolidation, amalgamation, share exchange, business combination, issuance of securities, acquisition of securities, reorganization, recapitalization, tender offer, exchange offer or other similar transaction involving a party to the Merger Agreement or any of its subsidiaries, except for Miragen s concurrent financing;

- any sale, lease, exchange, transfer, license, acquisition or disposition of any business or businesses or assets that constitute or account for 20% or more of the consolidated book value or the fair market value of the assets of a party and its subsidiaries, taken as a whole (other than the sale, divestiture and/or winding down of Signal s lab business in accordance with the terms and conditions of the Merger Agreement and any lease, exchange, transfer, license, disposition, partnership or collaboration involving less than substantially all of the assets of Miragen or any Miragen Subsidiary pursuant to a collaboration agreement, partnership agreement or similar arrangement); or

- any tender offer or exchange offer that if consummated would result in any person beneficially owning 20% or more of the outstanding equity securities of a party to the Merger Agreement or any of its subsidiaries.

A superior competing proposal is any unsolicited bona fide competing proposal (with all references to 20% in the definition of competing proposal being treated as references to 50% for these purposes) made by a third party that the board of directors of either Signal or Miragen, as the case may be, determines, in its reasonable, good faith judgment, after obtaining and taking into account such matters that its board of directors deems relevant following consultation

with its outside legal counsel and financial advisor, if any (i) is more favorable, from a financial point of view, to the Signal stockholders or the Miragen stockholders, as applicable, than the terms of the Merger; and (ii) is reasonably capable of being consummated; *provided*, *however*, that any such offer shall not be deemed to be a superior competing proposal if (A) any financing required to consummate the transaction contemplated by such offer is not committed and is not reasonably capable of being obtained by such third party or (B) if the consummation of such transaction is contingent on any such financing being obtained.

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Either Signal or Miragen, as the case may be, may terminate the Merger Agreement if the board of directors, and/or any committee of the board of directors, of the other party has (each such action, a change of recommendation by the board of directors and/or any committee of the board of directors of Signal or Miragen, as the case may be):

- failed to include its approval and recommendation to stockholders relating to the Merger in this proxy statement/prospectus/information statement;
- approved, endorsed or recommended a competing proposal; or
- entered into a definitive agreement for a competing proposal.

Either Signal or Miragen, as the case may be, may also terminate the Merger Agreement if it enters into a definitive agreement to effect a superior competing proposal. If the Merger Agreement is terminated in connection with these provisions, (i) Signal has agreed to pay Miragen a fee of $300,000, plus up to $100,000 as reimbursement for reasonable expenses, if the termination is a result of Signal entering into a definitive agreement to effect a superior competing proposal and (ii) Miragen has agreed to pay Signal a fee of $300,000, plus up to $100,000 as reimbursement for reasonable expenses if the termination is a result of Miragen entering into a definitive agreement to effect a superior competing proposal. See *The Merger Agreement Termination of the Merger Agreement and Termination Fee* below for a more complete discussion of the termination fees.

Disclosure Documents

As promptly as practicable following the date of the Merger Agreement, Signal agreed to prepare and file with the SEC this proxy statement/prospectus/information statement and Signal, in cooperation with Miragen, agreed to prepare and file with the SEC a registration statement on Form S-4, of which this proxy statement/prospectus/information statement is a part, in connection with the registration under the Securities Act of the shares of Signal common stock to be issued pursuant to the Merger. Each of Signal and Miragen agreed to use their commercially reasonable efforts to cause the registration statement to become effective as promptly as practicable, and take all or any action required under any applicable federal and state securities and other laws in connection with the issuance of shares of Signal common stock pursuant to the Merger. Each of Signal and Miragen agreed to use their commercially reasonable efforts to cause all documents that it is respectively responsible for filing with the SEC in connection with the transactions contemplated by the Merger Agreement to comply as to form and substance in all material respects with the applicable requirements of the Securities Act and the Securities Exchange Act of 1934, as amended, or the Exchange Act. Miragen agreed to ensure that its financial statements will comply as to form in all material respects, prior to the filing of the registration statement on Form S-4, with the published rules and regulations of the SEC with respect thereto. Each of Signal, Merger Sub and Miragen agreed to furnish all information concerning itself and its subsidiaries, as applicable, to the other parties as the other parties may reasonably request in connection with such actions and the preparation of the registration statement on Form S-4 and proxy statement/prospectus/information statement. Signal agreed to use commercially reasonable efforts to cause this proxy statement/prospectus/information statement to be mailed to its stockholders as promptly as practicable after the registration statement on Form S-4 is declared effective by the SEC.

Meeting of Signal Stockholders and Written Consent of Miragen s Stockholders

Signal is obligated under the Merger Agreement to call, give notice of and hold a meeting of its stockholders for the purposes of voting on the Signal Proposals. The Signal stockholders meeting will be held (on a date selected by Signal in consultation with Miragen) not later than 60 days after the effective date of the registration statement on Form S-4 pursuant to the Merger Agreement. If on the scheduled date of the Signal stockholders meeting, Signal has not obtained the requisite approval of its stockholders, Signal will have the right, after consultation with Miragen, to adjourn the stockholder meeting to a later date or dates, such later date or dates not to exceed 30 days from the original date that the stockholder meeting was scheduled.

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Miragen is obligated under the Merger Agreement to take all action necessary in accordance with the Merger Agreement, applicable law, and Miragen s restated certificate of incorporation and bylaws, to obtain, promptly after receiving written notice from Signal that the registration statement on Form S-4 registration statement has been declared effective under the Securities Act, and in any event no later than five business days after receiving such notice, adoption of the Merger Agreement and approval of the Merger by written consent of Miragen s stockholders.

Regulatory Approvals

Neither Signal nor Miragen is required to make any filings or to obtain approvals or clearances from any antitrust regulatory authorities in the United States or other countries to complete the Merger. In the United States, Signal must comply with applicable federal and state securities laws and the rules and regulations of The NASDAQ Stock Market LLC in connection with the issuance of shares of Signal s common stock in the Merger, including the filing with the SEC of this proxy statement/prospectus/information statement. The Merger Agreement provides that Miragen and Signal shall respond as promptly as is practicable in compliance with: (i) any inquiries or requests received from the Federal Trade Commission or the Department of Justice for information or documentation; and (ii) any inquiries or requests received from any other governmental body in connection with antitrust or competition matters.

Miragen Stock Options and Miragen Warrants

At the effective time of the Merger, each outstanding option and warrant, whether or not vested, to purchase Miragen capital stock unexercised immediately prior to the effective time of the Merger will be converted into an option or warrant to purchase Signal common stock. All rights with respect to each Miragen option or warrant will be assumed by Signal in accordance with its terms. Accordingly, from and after the effective time of the Merger each option or warrant assumed by Signal may be exercised solely for shares of Signal common stock.

The number of shares of Signal common stock subject to each outstanding Miragen option or warrant assumed by Signal will be determined by multiplying the number of shares of Miragen capital stock that were subject to such option or warrant, as applicable, by the Exchange Ratio and rounding the resulting number down to the nearest whole number of shares of Signal common stock. The per share exercise price for the Signal common stock issuable upon exercise of each Miragen option or warrant assumed by Signal will be determined by dividing the per share exercise price of Miragen capital stock subject to such option or warrant, as applicable, by the Exchange Ratio and rounding the resulting exercise price up to the nearest whole cent. Any restriction on the exercise of any option or warrant will continue in full force and effect and the term, exercisability, vesting schedule and other provisions of such option or warrant will otherwise remain unchanged.

Indemnification and Insurance for Officers and Directors

Under the Merger Agreement, from the closing of the Merger through the sixth anniversary of the closing, Signal and the surviving corporation agree that all rights to indemnification, exculpation or advancement of expenses now existing in favor of, and all limitations on the personal liability of, each present and former director or officer, of Signal or Miragen provided for in the respective organizational documents of Miragen and Signal in effect as of October 31, 2016, shall continue to be honored and in full force and effect.

Under the Merger Agreement, the certificate of incorporation and bylaws of Signal and the surviving corporation in the Merger, will contain provisions no less favorable with respect to indemnification, advancement of expenses and exculpation of present and former directors and officers of each of Signal and Miragen than are presently set forth in the certificate of incorporation and bylaws of Signal and Miragen, as applicable, which provisions shall not be amended, modified or repealed for a period of six years time from the closing of the Merger in a manner that would

materially and adversely affect the rights thereunder of individuals who, at or prior to the closing, were officers or directors of Signal and Miragen.

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The Merger Agreement also provides that Signal shall purchase an insurance policy in effect for six years from the closing, providing at least the same coverage as the current directors and officers liability insurance policies maintained by Miragen and Signal and containing terms and conditions that are not materially less favorable to current and former officers and directors of Miragen and Signal.

Additional Agreements

Each of Miragen and Signal has agreed to, among other things:

- use its commercially reasonable efforts to cause to be taken all actions necessary to consummate the Merger and any other transaction contemplated by the Merger Agreement;
- reasonably cooperate with the other parties and provide the other parties with such assistance as may be reasonably requested for the purpose of facilitating the performance by each party of its respective obligations under the Merger Agreement and to enable the surviving corporation to continue to meet its obligations under the Merger Agreement following the closing;
- make all filings and other submissions (if any) and give all notices (if any) required to be made and given by such party in connection with the Merger and any other transaction contemplated by the Merger Agreement;
- use its commercially reasonable efforts to lift any injunction prohibiting, or any other legal bar to, the Merger and any other transaction contemplated by the Merger Agreement;
- use its commercially reasonable efforts to satisfy the conditions precedent to the consummation of the Merger Agreement; and
- use its reasonable best efforts to cause the Merger to qualify as a reorganization under Section 368(a) of the Code.

NASDAQ Stock Market Listing

Signal common stock currently is listed on The NASDAQ Capital Market under the symbol SGNL. Signal has agreed to use commercially reasonable efforts to (i) maintain its existing listing on The NASDAQ Capital Market and to obtain approval of the listing of the combined company on The NASDAQ Capital Market, (ii) prepare and submit to The NASDAQ Capital Market a notification form for the listing of the shares of Signal common stock to be issued to Miragen stockholders pursuant to the Merger and the reverse split, (iii) cause such shares to be approved for listing and (iv) as required by NASDAQ Marketplace Rule 5110, file an initial listing application for the combined company on The NASDAQ Capital Market and to cause such listing application to be approved for listing. In addition, under the Merger Agreement, each of Miragen s and Signal s obligation to complete the Merger is subject to the satisfaction or waiver by each of the parties, at or prior to the Merger, of various conditions, including that the existing shares of Signal common stock must have been continually listed on The NASDAQ Capital Market, Signal must have caused the shares of Signal common stock to be issued in the Merger to be approved for listing on The NASDAQ Capital

Market as of the effective time of the Merger and, to the extent required by NASDAQ Marketplace Rule 5110, the initial listing application for the combined company must be approved for listing. If such application is accepted, Signal anticipates that its common stock will be listed on The NASDAQ Capital Market following the closing of the Merger under the trading symbol MGEN.

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Conditions to the Completion of the Merger

The respective obligations of Signal and Miragen to complete the Merger and the other transactions contemplated by the Merger Agreement are subject to the satisfaction or waiver of various conditions that (i) do not include the closing of Miragen s concurrent financing and (ii) do include, in addition to other customary closing conditions, the following:

- the registration statement on Form S-4, of which this proxy statement/prospectus/information statement is a part, must have been declared effective by the SEC in accordance with the Securities Act and must not be subject to any stop order or proceeding, or any proceeding threatened by the SEC, seeking a stop order;

- there must not have been issued any temporary restraining order, preliminary or permanent injunction or other order preventing the consummation of the Merger by any court of competent jurisdiction or other governmental entity of competent jurisdiction, and no law, statute, rule, regulation, ruling or decree shall be in effect which has the effect of making the consummation of the Merger illegal;

- the holders of a majority of the outstanding Miragen common stock and preferred stock, voting together as one class on an as-converted to common stock basis and 70% of the shares of Miragen preferred stock, voting together as one class on an as-converted to common stock basis, must have adopted and approved the Merger Agreement and the Merger;

- the holders of a majority of the shares of outstanding Signal common stock entitled to vote on the record date must have approved Signal Proposal Nos. 6, 7, 8 and 9;

- the holders of a majority of the shares having voting power and present in person or represented by proxy at the Signal special meeting must have approved Signal Proposal Nos. 1, 2, 3, 4, and 5;

- any waiting period applicable to the consummation of the Merger under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, or HSR Act, must have expired or been terminated, and there must not be in effect any voluntary agreement by any party to the Merger Agreement and the U.S. Federal Trade Commission, the U.S. Department of Justice or any foreign governmental body, pursuant to which such party has agreed not to consummate the Merger for any period of time; and

- the existing shares of Signal common stock must have been continually listed on The NASDAQ Capital Market through the closing of the Merger, the shares of Signal common stock to be issued in the Merger must be approved for listing on The NASDAQ Capital Market (subject to official notice of issuance) as of the effective time of the Merger, and the initial listing application of Miragen has been approved for listing.

In addition, each of Miragen s and Signal s obligation to complete the Merger is further subject to the satisfaction or waiver by that party of the following additional conditions:

the representations and warranties regarding capitalization matters of the other party in the Merger Agreement must be true and correct in all but de minimis respects on the date of the Merger Agreement and on the closing date of the Merger with the same force and effect as if made on the closing date, or, if such representations and warranties address matters as of a particular date, then as of that particular date;

all other representations and warranties of the other party in the Merger Agreement must be true and correct on the date of the Merger Agreement and on the closing date of the Merger with the same force and effect as if made on the date on which the Merger is to be completed or, if such representations and warranties address matters as of a particular date, then as of that particular date, except where the failure of these representations and warranties to be true and correct would not have a material adverse effect on the other party;

the other party to the Merger Agreement must have performed or complied with in all material respects all covenants and obligations in the Merger Agreement required to be performed or complied with by it on or before the closing of the Merger;

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the other party to the Merger Agreement has not experienced a material adverse effect; and

the other party must have delivered certain certificates and other documents required under the Merger Agreement for the closing of the Merger.

In addition, the obligation of Signal and Merger Sub to complete the Merger is further subject to the satisfaction or waiver of the following conditions:

Miragen must have effected a conversion of all of its outstanding preferred stock into shares of Miragen common stock;

Miragen must have terminated certain investor agreements; and

Miragen must have delivered a certificate setting forth the allocation of the Merger consideration to its securityholders.

In addition, the obligation of Miragen to complete the Merger is further subject to the satisfaction or waiver of the following conditions:

Signal must have terminated all contracts, subject to certain exceptions;

Signal must have appointed the directors and officers designated by Miragen;

either the principal executive officer or the principal financial officer of Signal must have provided, with respect to any document filed with the SEC on or after October 31, 2016, any necessary certification required under Rule 13a-14 under the Exchange Act, as amended;

the Signal Net Cash must be greater than or equal to negative $300,000. Net Cash means (i) the sum of Signal s cash and cash equivalents, marketable securities, accounts, interest and other receivables (to the extent determined to be collectible), and deposits (to the extent refundable to Signal), in each case as of the anticipated closing date, determined in a manner consistent with the manner in which such items were historically determined and in accordance with Signal s audited financial statements and Signal s unaudited interim balance sheet, *minus* (ii) the sum of Signal s accounts payable and accrued expenses (without duplication of any expenses accounted for below), in each case as of such date and determined in a manner consistent with the manner in which such items were historically determined and in accordance with Signal s audited financial statements and Signal s unaudited interim balance sheet, *minus* (iii) the cash cost of any unpaid change of control payments or severance, termination or similar payments that are or become due to any current or former employee, director or independent contractor of Signal, or any other third party *minus* (iv) the cash cost of any accrued and unpaid retention payments or other bonuses due to any current or former employee, director or independent contractor of Signal as of the closing date, *minus* (v) the cash cost

of any other payments to terminated Signal employees not set forth in clauses (iii) or (iv), *minus* (vi) all payroll, employment or other withholding taxes incurred by Signal and any Signal employee (to the extent paid or to be paid by Signal on the behalf of such employee) in connection with any payment amounts set forth in clauses (iii), (iv) or (v) and the exercise of any Signal option or settlement of any Signal restricted stock unit on or prior to the effective time, *minus* (vii) any remaining unpaid fees and expenses (including any attorney s, accountant s, financial advisor s or finder s fees) as of such date for which Signal is liable incurred by Signal in connection with the Merger Agreement and the Merger and other transactions contemplated by the Merger Agreement or otherwise, *minus* (viii) any bona fide current liabilities payable in cash, in each case to the extent not cancelled at or prior to the anticipated closing date, *minus* (ix) any fees and expenses payable by Signal pursuant to the Merger Agreement, *minus* (x) any unpaid amounts payable by Signal in satisfaction of its obligations under the Merger Agreement for the period after the closing (including any expenses incurred in connection with the tail policy), *minus* (xi) the cash cost of any unpaid retention payment amounts due under any insurance policy with respect to any legal proceeding against Signal or Merger Sub, *minus* (xii) the cash cost of repurchasing any shares of Signal common stock to the extent Signal has agreed to purchase such shares and the

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purchase price for such shares has not been fully paid by Signal as of the determination date, *plus* or *minus* (as applicable) (xiii) the net amount of any transaction expense reimbursements owed to, or transaction expense payment owed by, Signal pursuant to the Merger Agreement, *plus* (xiv) the amount of any payments due to Signal within 30 days of the closing date pursuant to the sale or other disposition of all or a portion of Signal s lab business, *plus* (xv) any amounts paid or payable by Signal for activities requested by Miragen in respect of the audit of Signal s financial statements at and for the year ended December 31, 2016, as well as for the preparation of Signal s Annual Report on Form 10-K for 2016;

Signal must have completed the sale, divestiture and/or winding down of its lab business such that there are no post-closing obligations of Signal remaining;

Signal must have satisfied all of its liabilities and received payoff letters authorizing the release of liens on its assets;

Signal must have effected the reverse stock split described in Signal Proposal No. 7;

Signal must have effected the conversion of the Note into shares of Signal common stock;

Signal s board of directors must have approved an amendment to the bylaws of Signal to prohibit the ability of Signal stockholders to act by written consent;

Signal must have delivered to Miragen written resignations of the officers and directors of Signal; and

Signal must have delivered a certificate setting forth and certifying the number of outstanding shares of its capital stock.

Termination of the Merger Agreement and Termination Fee

The Merger Agreement may be terminated at any time before the closing of the Merger, whether before or after the required stockholder approvals to complete the Merger have been obtained, as set forth below:

(1) By mutual agreement of Miragen and Signal;

(2) By either Miragen or Signal if the Merger has not closed by April 30, 2017 (other than in cases in which such failure to close is due to a breach by the party wishing to terminate), which date may be extended in certain circumstances;

(3) By either Miragen or Signal if there is any law or order that prohibits the completion of the Merger;

(4) By Signal if Miragen has not obtained the required vote from Miragen stockholders within five business days of the registration statement on Form S-4 of which this proxy statement/prospectus/information statement being is a part declared effective by the SEC;

(5) By either Miragen or Signal if the Signal special meeting has been held and completed and the required proposals have not been approved (other than in cases in which such failure has been caused by Signal s action or failure to act and such action or failure to act is a material breach by Signal);

(6) By Miragen (any time prior to obtaining the required from Signal stockholders) if (i) Signal failed to include its board recommendation of the proposals in this proxy statement/prospectus/information statement, (ii) the Signal board has approved, endorsed or recommended any competing proposal, (iii) Signal has failed to hold the Signal special meeting within 60 days of this proxy statement/prospectus/information statement being declared effective, (iv) Signal has entered into any definitive agreement for a competing proposal or (v) Signal has willfully and intentionally breached the non-solicitation obligations in the Merger Agreement;

(7) By Signal (any time prior to obtaining the required vote from Miragen stockholders) if (i) the Miragen board fails to include its board recommendation of the proposals in this proxy statement/prospectus/information statement, (ii) the Miragen board has approved, endorsed or recommended any competing

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proposal, (iii) Miragen has entered into any definitive agreement for a competing proposal or (iv) Miragen has willfully and intentionally breached the non-solicitation obligations in the Merger Agreement;

(8) By Miragen if Signal breaches any of its representations, warranties, covenants or agreements in the Merger Agreement that would prevent Signal from satisfying its closing conditions (with a 15 calendar day cure period);

(9) By Signal if Miragen breaches any of its representations, warranties, covenants or agreements in the Merger Agreement that would prevent Miragen from satisfying its closing conditions (with a 15 calendar day cure period);

(10) By Signal (prior to obtaining the required vote from Signal stockholders) if the Signal board authorizes Signal to enter into any definitive for a competing proposal that constitutes a superior competing proposal (so long as (i) Signal has complied with the non-solicitation and notification provisions in the Merger Agreement, (ii) Signal pays Miragen the termination fee and expenses reimbursable under the Merger Agreement and (iii) a copy of such agreement has been delivered to Miragen); or

(11) By Miragen (prior to obtaining the required vote by Miragen stockholders) if the Miragen board authorizes Miragen to enter into any definitive for a competing proposal that constitutes a superior competing proposal (so long as (i) Miragen has complied with the non-solicitation and notification provisions in the Merger Agreement, (ii) Miragen pays Signal the termination fee and any expenses reimbursable under the Merger Agreement and (iii) a copy of such agreement has been delivered to Signal).

Miragen is required to pay Signal a termination fee of $300,000 and expense reimbursements of up to $100,000, if the Merger Agreement is terminated by Signal pursuant to clauses 4, 7, or 11 above. Miragen is also required to pay Signal expense reimbursements of up to $100,000 if the Merger Agreement is terminated pursuant to clause 9 above or if there is a material adverse effect with respect to Miragen.

Signal is required to pay Miragen a termination fee of $300,000, and expense reimbursements of up to $100,000, if the Merger Agreement is terminated by Miragen pursuant to clauses 5, 6, or 10 above. Signal is also required to pay Miragen expense reimbursements of up to $100,000 if the Merger Agreement is terminated pursuant to clause 8 above or if there is material adverse effect with respect to Signal.

Any termination of the Merger Agreement shall not relieve any party of liability for any willful and material breach of any representation, warranty, covenant, obligation or other provision contained in the Merger Agreement.

Amendment

The Merger Agreement may be amended by an instrument in writing signed on behalf of each of Signal and Miragen with the approval of the respective boards of directors of Signal and Miragen at any time, except that after the Merger Agreement has been adopted by the stockholders of Signal or Miragen, no amendment which by law requires further approval by the stockholders of Signal or Miragen, as the case may be, shall be made without such further approval.

Expenses

The Merger Agreement provides all fees and expenses incurred in connection with the Merger Agreement and the transactions contemplated thereby shall be paid by the party incurring such expenses, except as described above under Termination of the Merger Agreement and Termination Fee and except that Miragen and Signal shall share equally in any fees and expenses incurred by the engagement of the exchange agent and in relation to printing and filing with the SEC of this proxy statement/prospectus/information statement.

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Directors and Officers of Signal Following the Merger

Pursuant to the Merger Agreement, effective as of the effective time of the Merger, the initial size of the board of directors of the combined company will be seven and the initial directors will be William S. Marshall, Ph.D., Bruce L. Booth, Ph.D., John W. Creecy, Thomas E. Hughes, Ph.D., Kevin Koch, Ph.D., Kyle A. Lefkoff and Joseph L. Turner.

The Merger Agreement also provides that, effective as of the effective time of the Merger, Signal shall appoint the following persons as officers of Signal: William S. Marshall, Ph.D. as president and chief executive officer, Jason A. Leverone as chief financial officer, treasurer and secretary, Adam S. Levy as chief business officer and Paul D. Rubin, M.D., as executive vice president, research and development.

Amendments to the Certificate of Incorporation of Signal

Signal agreed to submit to its stockholders, amendments to its certificate of incorporation, to, among other things:

change the name from Signal Genetics, Inc. to Miragen Therapeutics, Inc. ;

effect a reverse stock split of the outstanding shares of Signal common stock; and

eliminate the ability of Signal stockholders to act by written consent.

Each amendment to Signal s certificate of incorporation is subject to and conditioned upon the approval and completion of the Merger.

Special Meeting of Signal Stockholders

Signal is obligated under the Merger Agreement to call, give notice of and hold a special meeting of its stockholders for the purpose of considering the issuance of shares of Signal common stock, the Merger and the stockholder proposals discussed herein.

Miragen Written Consent

Miragen is obligated under the Merger Agreement to obtain written consents of its stockholders sufficient to adopt the Merger Agreement thereby approving the Merger and related transactions within five business days of the registration statement on Form S-4, of which this proxy statement/prospectus/information statement is a part, being declared effective by the SEC.

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AGREEMENTS RELATED TO THE MERGER

Subscription Agreement

On October 31, 2016, prior to the execution of the Merger Agreement, Miragen entered into the Subscription Agreement with certain current stockholders of Miragen and certain new investors in Miragen pursuant to which Miragen agreed to sell, and the purchasers listed therein agreed to purchase, an aggregate of 9,045,126 shares of Miragen common stock at a purchase price of $4.50 per share prior to the closing of the Merger for an aggregate purchase price of $40.7 million.

The consummation of the financing contemplated by the Subscription Agreement is subject to certain conditions, including the satisfaction or waiver of each of the conditions to the consummation of the Merger set forth in the Merger Agreement and the parties to the Merger Agreement being ready, willing and able to consummate the Merger immediately after the closing of the financing, which include, among other items, (i) the SEC having declared effective the registration statement on Form S-4 of which this proxy statement/prospectus/information statement is a part and no stop order suspending the effectiveness of the registration statement on Form S-4 of which this proxy statement/prospectus/information statement is a part having been issued and remain pending, and (ii) the approval of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8, and 9 by Signal stockholders.

The Subscription Agreement contains representations and warranties of Miragen comparable to the representations and warranties of Miragen in the Merger Agreement. The Subscription Agreement also contains customary representations and warranties of the purchasers.

Each purchaser s obligation to purchase shares of Miragen common stock from Miragen pursuant to the Subscription Agreement is subject to the satisfaction or waiver of certain conditions, including:

- Miragen s representations and warranties in the Subscription Agreement being true and correct in all respects as of October 31, 2016 and as of the closing date for the financing, except where the failure of such representations to be so true and correct would not have a material adverse effect on Miragen;
- Miragen having performed, satisfied and complied in all material respects with all covenants, agreements and conditions required to be performed, satisfied or complied with by it under the Subscription Agreement;
- the absence of any statute, rule, regulation, executive order, decree, ruling or injunction that prohibits the consummation of the sale of the shares to be sold in the financing;
- Miragen has obtained all consents and waivers necessary for the sale of the shares to be sold in the financing;
- Miragen has delivered to the purchasers, certain items at or prior to the closing of the financing;

each of the conditions to the consummation of the Merger set forth in the Merger Agreement having been satisfied or waived and the parties to the Merger Agreement being ready, willing and able to consummate the Merger immediately after the closing of the financing on the terms and conditions set forth therein; and

the actual subscription amount for each other purchaser under the Subscription Agreement having been released to Miragen in accordance with the Subscription Agreement.

Miragen s obligation to sell shares of Miragen common stock to each purchaser pursuant to the Subscription Agreement is subject to the satisfaction or waiver of certain conditions, including:

the representations and warranties made by such purchaser being true and correct in all material respects as of October 31, 2016 and as of the closing date for the financing, subject to certain exceptions;

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such purchaser having performed, satisfied and complied in all material respects with all covenants, agreements and conditions required to be performed, satisfied or complied with by such purchaser under the Subscription Agreement;

the absence of any statute, rule, regulation, executive order, decree, ruling or injunction that prohibits the consummation of the sale of the shares to be sold in the financing;

such purchaser s delivery to Miragen of certain items at or prior to the closing of the financing;

each of the conditions to the consummation of the Merger set forth in the Merger Agreement having been satisfied or waived and the parties to the Merger Agreement being ready, willing and able to consummate the Merger immediately after the closing of the financing on the terms and conditions set forth therein;

the actual subscription amount for each purchaser under the Subscription Agreement having been released to Miragen in accordance with the Subscription Agreement; and

the delivery to Miragen by Wedbush Securities Inc., Miragen s placement agent in the financing, of a questionnaire at or prior to the closing of the financing.

The representations and warranties contained in the Subscription Agreement will terminate at the closing of the financing and only the agreements and covenants that by their terms survive the closing of the financing will survive.

The Subscription Agreement may be amended and its provisions waived by Miragen and the purchasers party to the Subscription Agreement.

At any time prior to the closing of the financing, the Subscription Agreement may be terminated by any purchaser (with respect to itself only) by the mutual written consent of Miragen and such purchaser. The Subscription Agreement may also be terminated by any purchaser (with respect to itself only) if the closing of the financing or the Merger has not been consummated on or prior to 5:00 p.m., New York City time, on April 30, 2017, subject to certain exceptions. In addition, Miragen or any purchaser (with respect to itself only) may terminate the Subscription Agreement if the purchase and sale of the shares pursuant to the Subscription Agreement would violate any nonappealable order, degree or judgment of any governmental authority having competent jurisdiction.

Support Agreements

In connection with the execution of the Merger Agreement, Miragen s officers, directors and some stockholders of Miragen who collectively beneficially own or control approximately 78% of the voting power of Miragen s outstanding capital stock on an as-converted to common stock basis as of December 31, 2016 entered into support agreements with Signal under which such stockholders have agreed to vote in favor of the Merger and the Merger Agreement and against any competing transaction.

In connection with the execution of the Merger Agreement, Signal s officers, directors and some stockholders of Signal, who collectively beneficially own or control approximately 26% of Signal common stock as of December 31, 2016, also entered into support agreements with Miragen under which such stockholder has agreed to vote in favor of

the Signal Proposals and against any competing transaction.

Each stockholder executing a support agreement has made representations and warranties to Signal or Miragen, as applicable, regarding ownership and unencumbered title to the shares subject to such agreement, such stockholder s power and authority to execute the support agreement, due execution and enforceability of the support agreement, and ownership and unencumbered title to the shares. Unless otherwise waived, all of these support agreements prohibit the transfer, sale, assignment, gift or other disposition by the stockholder of their

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respective shares of Signal or Miragen capital stock, or the entrance into an agreement or commitment to do any of the foregoing, subject to specified exceptions. Each Miragen stockholder executing a support agreement has also waived its statutory appraisal rights in connection with the Merger.

The support agreements will terminate at the earlier of the effective time of the Merger or the termination of the Merger Agreement in accordance with its terms.

Lock-up Agreements

Miragen s officers, directors and certain other securityholders of Miragen also entered into lock-up agreements, pursuant to which such securityholders have agreed not to, except in limited circumstances, offer, pledge, sell, contract to sell, sell any option to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, any Miragen securities or shares of Signal common stock, including, as applicable, shares received in the Merger and issuable upon exercise of certain warrants and options, until 180 days after the closing date of the Merger.

The Miragen stockholders who have executed lock-up agreements as of December 31, 2016 owned, in the aggregate, approximately 98% of the shares of Miragen s outstanding capital stock on an as-converted to common stock basis.

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MATTERS BEING SUBMITTED TO A VOTE OF SIGNAL STOCKHOLDERS

Signal Proposal No. 1: Approval of the Issuance of Common Stock in the Merger

At the Signal special meeting, Signal stockholders will be asked to approve the issuance of Signal common stock pursuant to the Merger Agreement. Immediately following the Merger, it is expected that Miragen securityholders will own approximately 96% of the fully-diluted common stock of the combined company, with Signal securityholders owning approximately 4% of the fully-diluted common stock of the combined company, each assuming that Miragen closes its concurrent financing immediately prior to the effective time of the Merger. If the concurrent financing does not close, then Miragen securityholders would own approximately 94% of the fully-diluted common stock of the combined company and Signal securityholders would own approximately 6% of the fully-diluted common stock of the combined company. These estimates are based on the anticipated pre-split Exchange Ratio and post-split Exchange Ratios and are subject to adjustment.

The terms of, reasons for and other aspects of the Merger Agreement, the Merger and the issuance of Signal common stock pursuant to the Merger Agreement are described in detail in the sections titled *The Merger Agreement* and *The Merger*.

Required Vote

The affirmative vote of the holders of a majority of the shares of Signal common stock having voting power present in person or represented by proxy at the Signal special meeting is required to approve Signal Proposal No. 1. **Each of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9 are conditioned upon each other. Therefore, the Merger cannot be consummated without the approval of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9.**

Recommendation of Board of Directors

SIGNAL S BOARD OF DIRECTORS RECOMMENDS THAT THE SIGNAL STOCKHOLDERS VOTE FOR SIGNAL PROPOSAL NO. 1 TO APPROVE THE ISSUANCE OF SIGNAL COMMON STOCK PURSUANT TO THE MERGER AGREEMENT.

Signal Proposal No. 2: Approval of the Change of Control Resulting from the Merger

At the Signal special meeting, Signal stockholders will be asked to approve the change of control resulting from the Merger. Immediately following the Merger, it is expected that the Miragen securityholders will own approximately 96% of the fully-diluted common stock of the combined company, with Signal securityholders owning approximately 4% of the fully-diluted common stock of the combined company, each assuming that Miragen closes its concurrent financing immediately prior to the effective time of the Merger. If the concurrent financing does not close, then Miragen securityholders would own approximately 94% of the fully-diluted common stock of the combined company and Signal securityholders would own approximately 6% of the fully-diluted common stock of the combined company. These estimates are based on the anticipated pre-split Exchange Ratio and post-split Exchange Ratios and are subject to adjustment.

The terms of, reasons for and other aspects of the Merger Agreement, the Merger and the change of control resulting from the Merger are described in detail in the sections titled *The Merger Agreement* and *The Merger*.

Required Vote

The affirmative vote of the holders of a majority of the shares of Signal common stock having voting power present in person or represented by proxy at the Signal special meeting is required to approve Signal Proposal

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No. 2. **Each of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9 are conditioned upon each other. Therefore, the Merger cannot be consummated without the approval of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9.**

Recommendation of Board of Directors

SIGNAL S BOARD OF DIRECTORS RECOMMENDS THAT THE SIGNAL STOCKHOLDERS VOTE FOR SIGNAL PROPOSAL NO. 2 TO APPROVE THE CHANGE IN CONTROL RESULTING FROM THE MERGER.

Signal Proposal No. 3: Approval of the Conversion of the Note

At the Signal special meeting, Signal stockholders will be asked to approve the Note Amendment. Signal and Mr. LeBow entered into the Note Amendment in order to make the outstanding principal balance and accrued interest under the note convertible into shares of Signal common stock immediately prior to the effective time of the Merger. The conversion price is equal to the closing price of Signal s common stock on The NASDAQ Capital Market on October 31, 2016, the date that Signal and Mr. LeBow entered into the Note Amendment. By amending the Note to make it convertible into shares of Signal common stock, it eliminates the need for Signal to use its cash resources to pay the Note and allows Signal to better manage its cash resources to meet the closing net cash requirement contained in the Merger Agreement. Because the Note Amendment is a related party transaction, Signal is seeking stockholder approval and ratification of the conversion feature of the Note Amendment to comply with the listing rules of The NASDAQ Capital Market requiring stockholder approval of specified related party transactions.

Background of the Note

In connection with Signal s initial public offering in 2014, Mr. LeBow advanced $1,000,000 to Signal to pay for certain offering expenses. Following the offering, this amount, along with an additional $45,000, which was advanced to pay for certain additional offering expenses, was reclassified as amounts due to related party on Signal s consolidated balance sheet. This aggregate amount was non-interest bearing and due on demand.

On March 6, 2015, Signal s amounts due to a related party, an aggregate of $1,045,000, were converted into an unsecured note payable-related party bearing interest at 8% per annum and due on demand. The principal amount of the Note was also increased by $60,000 over the amounts due to related party to $1,105,009 to provide the equivalent of 8% per annum interest for the period of time the amounts due to related party were held as a payable in exchange for a provision that the related party would not call the Note prior to June 30, 2015. The increase in the principal amount of the Note was deferred and amortized to interest expense over the initial term of the Note to June 30, 2015. When issued, the terms of the original promissory note provided (i) for a principal amount of $1,105,009 which accrued interest computed on the basis of the actual number of days elapsed in a 360-day year, at a rate per annum of 8%, (ii) that at any time on or after June 30, 2015, Mr. LeBow may demand payment of the entire outstanding principal of the Note and all unpaid interest accrued thereon and (iii) that upon the occurrence and during the continuance of any event of default by Signal under the Note, the principal balance of the Note will accrue interest at a rate of 11%. The Note also contains customary representations and warranties of Signal, the breach of which would be among an event of default therein.

Interest expense related to this note during the three months and nine months ended September 30, 2016 was $22,000 and $66,000, respectively. The Note balance at September 30, 2016 was $1,105,009. Accrued interest payable of $139,000 is included in accrued liabilities in the balance sheet at September 30, 2016. No interest has been paid and as of the date of this proxy statement/prospectus/information statement, the Note has not been called.

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Note Amendment

On October 31, 2016, prior to the execution of the Merger Agreement, Signal and Mr. LeBow entered into the Note Amendment. The Note Amendment (i) makes the outstanding principal balance and all accrued interest on the note, plus a premium of 11% on the outstanding balance, automatically convertible into shares of Signal s common stock immediately prior to the effective time of the Merger at a conversion price of $5.39 per share, which is the closing price of Signal s common stock on The NASDAQ Capital Market on the effective date of the Note Amendment and (ii) modifies the principal amount of the original note to $1,045,000, the original amount advanced to Signal as of June 17, 2014, and the interest of the original note to a rate per annum of 11% commencing on June 17, 2014, with interest computed on the basis of the actual number of days in a 360-day year.

The conversion price is subject to appropriate adjustment in the event of any reverse stock split, forward stock split, stock dividend, combination or other similar recapitalization with respect to Signal s common stock. Conversion of the Note is subject to and conditioned upon Signal obtaining stockholder approval of any such conversion.

If conversion of the Note is not approved by Signal stockholders at the special meeting, or if the Merger Agreement is terminated prior to completion of the Merger, the outstanding balance due under the note will not be converted into Signal common stock and the note will remain outstanding. Moreover, because conversion of the outstanding balance of the note into shares of Signal common stock is a closing condition of the Merger Agreement, success of the Merger is also dependent upon stockholder approval of conversion of the Note.

Signal s board of directors, including the members of the board s audit committee who review and consider all related party transactions, determined that the Note Amendment was in Signal s best interest and approved the terms thereof. See the section titled *Principal Stockholders of Signal* in this proxy statement/prospectus/information statement for more information regarding the Signal common stock beneficially owned by Mr. LeBow.

Required Vote

The affirmative vote of the holders of a majority of the shares of Signal common stock having voting power present in person or represented by proxy at the Signal special meeting is required to approve Signal Proposal No. 3. **Each of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9 are conditioned upon each other. Therefore, the Merger cannot be consummated without the approval of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9.**

Recommendation of Board of Directors

SIGNAL S BOARD OF DIRECTORS RECOMMENDS THAT THE SIGNAL STOCKHOLDERS VOTE FOR SIGNAL PROPOSAL NO. 3 TO APPROVE THE CONVERSION OF THE NOTE INTO SHARES OF SIGNAL COMMON STOCK.

Signal Proposal No. 4: Approval of the Signal 2016 Equity Incentive Plan

The board of directors of Signal has approved the adoption of the Signal 2016 Equity Incentive Plan, or the 2016 Plan, subject to approval by Signal stockholders. In this Signal Proposal No. 4, Signal s board of directors is requesting stockholder approval of the 2016 Plan.

Approval of the 2016 Plan by Signal stockholders is required, among other things, in order to: (i) comply with NASDAQ rules requiring stockholder approval of equity compensation plans; (ii) allow the grant of incentive stock options to participants in the 2016 Plan and (iii) give the compensation committee of the combined company the

ability to grant awards intended to qualify as performance-based compensation, thereby potentially preserving combined company s tax deduction under Code Section 162(m).

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The discussion that follows is qualified in all respects to the terms of the 2016 Plan. A copy of the 2016 Plan is attached as *Annex B* to this proxy statement/prospectus/information statement. Signal stockholders should refer to the 2016 Plan for more complete and detailed information about the terms and conditions of the 2016 Plan.

If this Signal Proposal No. 4 is approved by Signal stockholders, the 2016 Plan will become effective as of the date of the closing of the Merger, and no further grants will be made under Signal s 2014 Stock Incentive Plan, or the 2014 Plan, or the Miragen Therapeutics, Inc. 2008 Equity Incentive Plan, or the Miragen 2008 Plan. In the event that Signal stockholders do not approve this proposal, the 2016 Plan will not become effective and the 2014 Plan and the Miragen 2008 Plan will continue to be effective in accordance with their terms and the combined company may continue to make awards under such plans, subject to the limits thereunder. Approval of the 2016 Plan by Signal stockholders will allow the combined company to grant stock options, restricted stock unit awards and other awards at levels determined appropriate by its board of directors or compensation committee following the closing of the Merger. The 2016 Plan will also allow the combined company to utilize a broad array of equity incentives and performance cash incentives in order to secure and retain the services of its employees, directors and consultants, and to provide long-term incentives that align the interests of its employees, directors and consultants with the interests of its stockholders following the closing of the Merger.

The combined company s employee equity compensation program, as implemented under the 2016 Plan, will allow the combined company to remain competitive with comparable companies in its industry by giving it the resources to attract and retain talented individuals to continue to achieve its business objectives and build stockholder value. Approval of the 2016 Plan will provide the combined company with the flexibility it needs to use equity compensation and other incentive awards to attract, retain and motivate talented employees, directors and independent contractors who are important to the combined company s long-term growth and success.

Best Practices Integrated into Signal s Equity Compensation Program and the 2016 Plan

The 2016 Plan includes provisions that are designed to protect the interests of the stockholders of the combined company and to reflect corporate governance best practices including:

No single trigger accelerated vesting upon change in control. The 2016 Plan does not provide for automatic vesting of awards upon a change in control.

Awards subject to forfeiture/clawback. Awards granted under the 2016 Plan will be subject to recoupment in accordance with any clawback policy that the combined company is required to adopt pursuant to the listing standards of any national securities exchange or association on which its securities are listed or as is otherwise required by the Dodd-Frank Wall Street Reform and Consumer Protection Act or other applicable law. In addition, the combined company may impose other clawback, recovery or recoupment provisions in an award agreement, including a reacquisition right in respect of previously acquired shares or other cash or property upon the occurrence of cause.

Repricing is not allowed. The 2016 Plan prohibits the repricing of outstanding stock options and stock appreciation rights and the cancellation of any outstanding stock options or stock appreciation rights that have an exercise or strike price greater than the then-current fair market value of a share of common stock in exchange for cash or other stock awards under the 2016 Plan without prior stockholder approval.

No liberal change in control definition. The change in control definition in the 2016 Plan is not a liberal definition. A change in control transaction must actually occur in order for the change in control provisions in the 2016 Plan to be triggered.

No discounted stock options or stock appreciation rights. All stock options and stock appreciation rights granted under the 2016 Plan must have an exercise or strike price equal to or greater than the fair market value of a share of common stock on the date the stock option or stock appreciation right is granted.

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Administration by independent committee. The 2016 Plan will be administered by the members of the combined company s compensation committee, all of whom are non-employee directors within the meaning of Rule 16b-3 under the Exchange Act and independent within the meaning of the listing standards of The NASDAQ Capital Market. In addition, all of the members of the combined company s compensation committee, which has been delegated certain authorities with respect to awards that are intended to qualify as performance-based compensation under Section 162(m) of the Code, are outside directors within the meaning of Section 162(m) of the Code.

Material amendments require stockholder approval. Consistent with the rules and regulations of The NASDAQ Stock Market LLC, the 2016 Plan requires stockholder approval of any material revisions to the 2016 Plan. In addition, certain other amendments to the 2016 Plan require stockholder approval.

Limit on non-employee director awards and other awards. Except in extraordinary circumstances, the maximum number of shares subject to stock awards granted under the 2016 Plan or otherwise during any calendar year to any of Signal s non-employee directors, taken together with any cash fees paid by the combined company to such non-employee director during such calendar year for service on the combined company s board of directors, may not exceed $500,000 in total value (calculating the value of any such stock awards based on the grant date fair value of such stock awards for financial reporting purposes), or with respect to the calendar year in which a non-employee director is first appointed or elected to the board, $1,000,000. The 2016 Plan also contains other annual per-participant limits on stock options, stock appreciation rights and performance-based stock and cash awards.

Information Regarding Equity Incentive Program

As discussed above, all outstanding stock options and restricted stock units held by Signal employees, directors and consultants, will be cancelled and terminated at the effective time of the Merger. In addition, all outstanding options with respect to shares of Miragen common stock will be assumed by Signal at the effective time of the Merger. As employees, directors and consultants of Miragen will continue in service with the combined company following the closing date of the Merger, Signal s board of directors believes that information regarding Miragen s equity grant practices may be most beneficial to Signal stockholders in connection with considering whether to approve the 2016 Plan.

It is critical to the combined company s long-term success that the interests of its employees, directors and consultants are tied to its success as owners of the business. Approval of the 2016 Plan will allow the combined company to continue to grant stock options and other equity awards at levels it determines to be appropriate in order to attract new employees and directors, retain existing employees and directors and to provide incentives for such persons to exert maximum efforts for the combined company s success and ultimately increase stockholder value. The 2016 Plan allows the combined company to continue to utilize a broad array of equity incentives with flexibility in designing equity incentives, including traditional stock option grants, stock appreciation rights, restricted stock awards, restricted stock unit awards, other stock awards and performance stock awards to offer competitive equity compensation packages in order to retain and motivate the talent necessary

If Signal s request to approve the 2016 Plan is approved by Signal stockholders, the combined company will have approximately 1,681,294 shares, subject to adjustment for specified changes in the combined company s capitalization and for the reverse stock split available for grant under the 2016 Plan as of the effective time of the closing of the Merger. In addition, as further described below under the section titled *Description of the 2016 Equity Incentive*

Plan Shares Available for Awards, up to an additional 2,501,110 shares, subject to adjustment for specified changes in the combined company s capitalization and for the reverse stock split, of the combined company s common stock that are subject to previously granted and outstanding awards under the Miragen 2008 Plan may become available for issuance under the 2016 Plan following the closing date if those awards are forfeited or the shares are not issued pursuant to the awards, and the share reserve is subject to annual increases each January 1 of up to 4% of shares of the combined company s common stock outstanding (or a lesser number

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determined by the combined company s board of directors). This pool size is necessary to provide sufficient reserved shares for a level of grants that will attract, retain, and motivate employees and other participants.

Performance-Based Awards

Approval of the 2016 Plan by Signal stockholders will also constitute approval of terms and conditions set forth therein that will permit the combined company to grant stock options, stock appreciation rights and performance-based stock and cash awards under the 2016 Plan that may qualify as performance-based compensation within the meaning of Section 162(m) of the Code. Section 162(m) of the Code disallows a deduction to any publicly held corporation and its affiliates for certain compensation paid to covered employees in a taxable year to the extent that compensation to a covered employee exceeds $1 million. However, some kinds of compensation, including qualified performance-based compensation, are not subject to this deduction limitation. For compensation awarded under a plan to qualify as performance-based compensation under Section 162(m) of the Code, among other things, the following terms must be disclosed to and approved by the stockholders before the compensation is paid: (i) a description of the employees eligible to receive such awards; (ii) a per-person limit on the number of shares subject to stock options, stock appreciation rights and performance-based stock awards, and the amount of cash subject to performance-based cash awards, that may be granted to any employee under the plan in any year; and (iii) a description of the business criteria upon which the performance goals for performance-based awards may be granted (or become vested or exercisable). Accordingly, Signal is requesting that Signal stockholders approve the 2016 Plan, which includes terms and conditions regarding eligibility for awards, annual per-person limits on awards and the business criteria for performance-based awards granted under the 2016 Plan (as described in the summary below).

Signal believes it is in the best interests of Signal stockholders to preserve the ability to grant performance-based compensation under Section 162(m) of the Code. However, in certain circumstances, the combined company may determine to grant compensation to covered employees that is not intended to qualify as performance-based compensation for purposes of Section 162(m) of the Code. Moreover, even if the combined company grants compensation that is intended to qualify as performance-based compensation for purposes of Section 162(m) of the Code, neither Signal nor the combined company can guarantee that such compensation ultimately will be deductible by Signal or the combined company.

Description of the 2016 Equity Incentive Plan

The material features of the 2016 Plan are described below. The following description of the 2016 Plan is a summary only and is qualified in its entirety by reference to the complete text of the 2016 Plan. Stockholders are urged to read the actual text of the 2016 Plan in its entirety.

Purpose

The 2016 Plan is designed to secure and retain the services of the combined company s employees, directors and consultants, provide incentives for Signal employees, directors and consultants to exert maximum efforts for the success of the combined company and its affiliates, and provide a means by which the combined company s employees, directors and consultants may be given an opportunity to benefit from increases in the value of its common stock. If the 2016 Plan is approved by Signal stockholders, no additional awards will be granted under the 2014 Plan or the Miragen 2008 Plan following the effective date of the 2016 Plan.

Types of Awards

The terms of the 2016 Plan provide for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, other stock awards, and performance awards that may be settled in cash, stock, or other property.

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Shares Available for Awards

Subject to adjustment for specified changes in the combined company s capitalization and for the reverse stock split, the aggregate number of shares of Signal common stock that may be issued under the 2016 Plan, or the Share Reserve, will not exceed 4,182,404 shares, which number is the sum of (i) 1,681,294 shares, plus (ii) the number of shares subject to outstanding stock awards that were granted under the Miragen 2008 Plan that, from and after the closing date of the Merger, expire or terminate for any reason prior to exercise or settlement, are forfeited because of the failure to meet a contingency or condition required to vest such shares, or are reacquired, withheld or not issued to satisfy a tax withholding obligation in connection with an award or to satisfy the purchase price or exercise price of a stock award, if any, as such shares become available from time to time. In addition, the share reserve will automatically increase on January 1st of each year, for a period of not more than ten years, commencing on January 1st of the year following the year in which the effective date of the 2016 Plan occurs, and ending on (and including) January 1, 2026, in an amount equal to 4% of the shares of common stock outstanding on December 31st of the preceding calendar year; however the board of directors or compensation committee may act prior to January 1st of a given year to provide that there will be no January 1st increase in the share reserve for such year or that the increase in the share reserve for such year will be a lesser number of shares of common stock than would otherwise occur pursuant to the automatic increase.

The following shares of common stock will become available again for issuance under the 2016 Plan: (i) any shares subject to a stock award that are not issued because such stock award expires or otherwise terminates without all of the shares covered by such stock award having been issued; (ii) any shares subject to a stock award that are not issued because such stock award is settled in cash; (iii) any shares issued pursuant to a stock award that are forfeited back to or repurchased by Signal because of the failure to meet a contingency or condition required for the vesting of such shares; and (iv) any shares reacquired by the combined company in satisfaction of tax withholding obligations on a stock award or as consideration for the exercise or purchase price of a stock award.

Eligibility

All of the combined company s (including its affiliates) approximately 45 employees and six non-employee directors as of December 31, 2016 will be eligible to participate in the 2016 Plan following the closing of the Merger and may receive all types of awards other than incentive stock options. Incentive stock options may be granted under the 2016 Plan only to the combined company s employees (including officers) and employees of its affiliates.

Section 162(m) Limits

Under the 2016 Plan, subject to adjustment for specified changes in the combined company s capitalization and for the reverse stock split, no participant will be eligible to be granted performance-based compensation during any calendar year more than: (i) a maximum of 1,500,000 shares of common stock subject to stock options and stock appreciation rights whose value is determined by reference to an increase over an exercise or strike price of at least 100% of the fair market value of a share of common stock on the date of grant; (ii) a maximum of 1,500,000 shares of common stock subject to performance stock awards; and (iii) a maximum of $3,000,000 subject to performance cash awards. These limits are designed to allow the combined company to grant awards that are intended to be exempt from the $1 million limitation on the income tax deductibility of compensation paid per covered employee imposed by Section 162(m) of the Code, and will not apply to awards that the combined company s board of directors determines will not be treated as performance-based compensation.

Non-Employee Director Compensation Limit

Under the 2016 Plan, the maximum number of shares of Signal common stock subject to stock awards granted under the 2016 Plan or otherwise during any one calendar year to any non-employee director, taken together with

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any cash fees paid by the combined company to such non-employee director during such calendar year for services on its board of directors, will not exceed $500,000 in total value (calculating the value of any such stock awards based on the grant date fair value of such stock awards for financial reporting purposes), or, with respect to the calendar year in which a non-employee director is first appointed or elected to the combined company s board of directors, $1,000,000.

Administration

The 2016 Plan will be administered by the combined company s board of directors, which may in turn delegate authority to administer the 2016 Plan to a committee. The combined company s board of directors will delegate concurrent authority to administer the 2016 Plan to its compensation committee, but may, at any time, revest in itself some or all of the power delegated to its compensation committee. The combined company s board of directors and its compensation committee are each considered to be a Plan Administrator for purposes of this Signal Proposal No. 4. Subject to the terms of the 2016 Plan, the Plan Administrator may determine the recipients, the types of awards to be granted, the number of shares of common stock subject to or the cash value of awards, and the terms and conditions of awards granted under the 2016 Plan, including the period of their exercisability and vesting. The Plan Administrator also has the authority to provide for accelerated exercisability and vesting of awards. Subject to the limitations set forth below, the Plan Administrator also determines the fair market value applicable to a stock award and the exercise or strike price of stock options and stock appreciation rights granted under the 2016 Plan.

The Plan Administrator may also delegate to one or more officers the authority to designate employees who are not officers to be recipients of certain stock awards and the number of shares of common stock subject to such stock awards. Under any such delegation, the Plan Administrator will specify the total number of shares of common stock that may be subject to the stock awards granted by such officer. The officer may not grant a stock award to himself or herself.

Repricing; Cancellation and Re-Grant of Stock Awards

Under the 2016 Plan, the Plan Administrator does not have the authority to reprice any outstanding stock option or stock appreciation right by reducing the exercise or strike price of the stock option or stock appreciation right or to cancel any outstanding stock option or stock appreciation right that has an exercise or strike price greater than the then-current fair market value of a share of common stock in exchange for cash or other stock awards without obtaining the approval of the combined company s stockholders. Such approval must be obtained within 12 months prior to such an event.

Stock Options

Stock options may be granted under the 2016 Plan pursuant to stock option agreements. The 2016 Plan permits the grant of stock options that are intended to qualify as incentive stock options, or ISOs, and nonstatutory stock options, or NSOs.

The exercise price of a stock option granted under the 2016 Plan may not be less than 100% of the fair market value of the common stock subject to the stock option on the date of grant and, in some cases (see *Limitations on Incentive Stock Options* below), may not be less than 110% of such fair market value.

The term of stock options granted under the 2016 Plan may not exceed ten years and, in some cases (see *Limitations on Incentive Stock Options* below), may not exceed five years. Except as otherwise provided in a participant s stock option agreement or other written agreement with the combined company or one of its affiliates, if a participant s service relationship with combined company or any of its affiliates, referred to in this Signal Proposal No. 4 as

continuous service, terminates (other than for cause and other than upon the participant s death or disability), the participant may exercise any vested stock options for up to three months

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following the participant s termination of continuous service. Except as otherwise provided in a participant s stock option agreement or other written agreement with the combined company or one of its affiliates, if a participant s continuous service terminates due to the participant s disability or death (or the participant dies within a specified period, if any, following termination of continuous service), the participant, or his or her beneficiary, as applicable, may exercise any vested stock options for up to 12 months following the participant s termination due to the participant s disability or for up to 18 months following the participant s death. Except as explicitly provided otherwise in a participant s stock option agreement or other written agreement with the combined company or one of its affiliates, if a participant s continuous service is terminated for cause (as defined in the 2016 Plan), all stock options held by the participant will terminate upon the participant s termination of continuous service and the participant will be prohibited from exercising any stock option from and after such termination date. Except as otherwise provided in a participant s stock option agreement or other written agreement with the combined company or one of its affiliates, the term of a stock option may be extended if the exercise of the stock option following the participant s termination of continuous service (other than for cause and other than upon the participant s death or disability) would be prohibited by applicable securities laws or if the sale of any common stock received upon exercise of the stock option following the participant s termination of continuous service (other than for cause) would violate Signal s insider trading policy. In no event, however, may a stock option be exercised after its original expiration date.

Acceptable forms of consideration for the purchase of common stock pursuant to the exercise of a stock option under the 2016 Plan will be determined by the Plan Administrator and may include payment: (i) by cash, check, bank draft or money order payable to the combined company; (ii) pursuant to a program developed under Regulation T as promulgated by the Federal Reserve Board; (iii) by delivery to the combined company of shares of common stock (either by actual delivery or attestation); (iv) by a net exercise arrangement (for NSOs only); or (v) in other legal consideration approved by the Plan Administrator.

Stock options granted under the 2016 Plan may become exercisable in cumulative increments, or vest, as determined by the Plan Administrator at the rate specified in the stock option agreement. Shares covered by different stock options granted under the 2016 Plan may be subject to different vesting schedules as the Plan Administrator may determine.

The Plan Administrator may impose limitations on the transferability of stock options granted under the 2016 Plan in its discretion. Generally, a participant may not transfer a stock option granted under the 2016 Plan other than by will or the laws of descent and distribution or, subject to approval by the Plan Administrator, pursuant to a domestic relations order or an official marital settlement agreement. However, the Plan Administrator may permit transfer of a stock option in a manner that is not prohibited by applicable tax and securities laws. In addition, subject to approval by the Plan Administrator, a participant may designate a beneficiary who may exercise the stock option following the participant s death.

Limitations on Incentive Stock Options

The aggregate fair market value, determined at the time of grant, of shares of common stock with respect to ISOs that are exercisable for the first time by a participant during any calendar year under all of the combined company s stock plans may not exceed $100,000. The stock options or portions of stock options that exceed this limit or otherwise fail to qualify as ISOs are treated as NSOs. No ISO may be granted to any person who, at the time of grant, owns or is deemed to own stock possessing more than 10% of Signal s total combined voting power or that of any affiliate unless the following conditions are satisfied:

the exercise price of the ISO must be at least 110% of the fair market value of the common stock subject to the ISO on the date of grant; and

the term of the ISO must not exceed five years from the date of grant.

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Subject to adjustment for specified changes in capitalization and for the reverse stock split, the aggregate maximum number of shares of common stock that may be issued pursuant to the exercise of ISOs under the 2016 Plan is 20,912,020 shares.

Stock Appreciation Rights

Stock appreciation rights may be granted under the 2016 Plan pursuant to stock appreciation right agreements. Each stock appreciation right is denominated in common stock share equivalents. The strike price of each stock appreciation right will be determined by the Plan Administrator, but will in no event be less than 100% of the fair market value of the common stock subject to the stock appreciation right on the date of grant. The Plan Administrator may also impose restrictions or conditions upon the vesting of stock appreciation rights that it deems appropriate. The appreciation distribution payable upon exercise of a stock appreciation right may be paid in shares of Signal common stock, in cash, in a combination of cash and stock, or in any other form of consideration determined by the Plan Administrator and set forth in the stock appreciation right agreement. Stock appreciation rights will be subject to the same conditions upon termination of continuous service and restrictions on transfer as stock options under the 2016 Plan.

Restricted Stock Awards

Restricted stock awards may be granted under the 2016 Plan pursuant to restricted stock award agreements. A restricted stock award may be granted in consideration for cash, check, bank draft or money order payable to the combined company, the participant s services performed for the combined company or any of its affiliates, or any other form of legal consideration acceptable to the Plan Administrator. Shares of common stock acquired under a restricted stock award may be subject to forfeiture to or repurchase by the combined company in accordance with a vesting schedule to be determined by the Plan Administrator. Rights to acquire shares of common stock under a restricted stock award may be transferred only upon such terms and conditions as are set forth in the restricted stock award agreement. A restricted stock award agreement may provide that any dividends paid on restricted stock will be subject to the same vesting conditions as apply to the shares subject to the restricted stock award. Upon a participant s termination of continuous service for any reason, any shares subject to restricted stock awards held by the participant that have not vested as of such termination date may be forfeited to or repurchased by the combined company.

Restricted Stock Unit Awards

Restricted stock unit awards may be granted under the 2016 Plan pursuant to restricted stock unit award agreements. Payment of any purchase price may be made in any form of legal consideration acceptable to the Plan Administrator. A restricted stock unit award may be settled by the delivery of shares of Signal common stock, in cash, in a combination of cash and stock, or in any other form of consideration determined by the Plan Administrator and set forth in the restricted stock unit award agreement. Restricted stock unit awards may be subject to vesting in accordance with a vesting schedule to be determined by the Plan Administrator. Dividend equivalents may be credited in respect of shares of common stock covered by a restricted stock unit award, provided that any additional shares credited by reason of such dividend equivalents will be subject to all of the same terms and conditions of the underlying restricted stock unit award. Except as otherwise provided in a participant s restricted stock unit award agreement or other written agreement with the combined company or one of its affiliates, restricted stock units that have not vested will be forfeited upon the participant s termination of continuous service for any reason.

Performance Awards

The 2016 Plan allows the combined company to grant performance stock and cash awards, including such awards that may qualify as performance-based compensation that is not subject to the $1 million limitation on the income tax deductibility of compensation paid per covered employee imposed by Section 162(m) of the Code.

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A performance stock award is a stock award that is payable (including that may be granted, may vest, or may be exercised) contingent upon the attainment of pre-determined performance goals during a performance period. A performance stock award may require the completion of a specified period of continuous service. The length of any performance period, the performance goals to be achieved during the performance period, and the measure of whether and to what degree such performance goals have been attained will be determined by the compensation committee of the combined company s board of directors, except that the Plan Administrator also may make any such determinations to the extent that the award is not intended to qualify as performance-based compensation under Section 162(m) of the Code. In addition, to the extent permitted by applicable law and the performance stock award agreement, the Plan Administrator may determine that cash may be used in payment of performance stock awards.

A performance cash award is a cash award that is payable contingent upon the attainment of pre-determined performance goals during a performance period. A performance cash award may require the completion of a specified period of continuous service. The length of any performance period, the performance goals to be achieved during the performance period, and the measure of whether and to what degree such performance goals have been attained will be determined by the compensation committee of the combined company s board of directors, except that the Plan Administrator also may make any such determinations to the extent that the award is not intended to qualify as performance-based compensation under Section 162(m) of the Code. The Plan Administrator may specify the form of payment of performance cash awards, which may be cash or other property, or may provide for a participant to have the option for his or her performance cash award to be paid in cash or other property.

In granting a performance stock or cash award intended to qualify as performance-based compensation under Section 162(m) of the Code, the compensation committee of the combined company s board of directors will set a period of time, or a performance period, over which the attainment of one or more goals, or performance goals, will be measured. Within the time period prescribed by Section 162(m) of the Code (no later than the earlier of the 90th day of a performance period and the date on which 25% of the performance period has elapsed, and in any event at a time when the achievement of the performance goals remains substantially uncertain), the compensation committee of the combined company s board of directors will establish the performance goals, based upon one or more criteria, or performance criteria, enumerated in the 2016 Plan and described below. As soon as administratively practicable following the end of the performance period, the compensation committee of the combined company s board of directors will certify in writing whether the performance goals have been satisfied.

Performance goals under the 2016 Plan will be based on any one or more of the following performance criteria: (i) earnings (including earnings per share and net earnings); (ii) earnings before interest, taxes and depreciation; (iii) earnings before interest, taxes, depreciation and amortization; (iv) earnings before interest, taxes, depreciation, amortization and legal settlements; (v) earnings before interest, taxes, depreciation, amortization, legal settlements and other income (expense); (vi) earnings before interest, taxes, depreciation, amortization, legal settlements, other income (expense) and stock-based compensation; (vii) earnings before interest, taxes, depreciation, amortization, legal settlements, other income (expense), stock-based compensation and changes in deferred revenue; (viii) earnings before interest, taxes, depreciation, amortization, legal settlements, other income (expense), stock-based compensation, other non-cash expenses and changes in deferred revenue; (ix) total stockholder return; (x) return on equity or average stockholder s equity; (xi) return on assets, investment, or capital employed; (xii) stock price; (xiii) margin (including gross margin); (xiv) income (before or after taxes); (xv) operating income; (xvi) operating income after taxes; (xvii) pre-tax profit; (xviii) operating cash flow; (xix) sales or revenue targets; (xx) increases in revenue or product revenue; (xxi) expenses and cost reduction goals; (xxii) improvement in or attainment of working capital levels; (xxiii) economic value added (or an equivalent metric); (xxiv) market share; (xxv) cash flow; (xxvi) cash flow per share; (xxvii) cash balance; (xxviii) cash burn; (xxix) cash collections; (xxx) share price performance; (xxxi) debt reduction; (xxxii) implementation or completion of projects or processes (including, without limitation, clinical trial initiation, clinical trial enrollment and dates, clinical trial results, regulatory filing submissions, regulatory filing

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acceptances, regulatory or advisory committee interactions, regulatory approvals, new and supplemental indications for existing products, and product supply); (xxxiii) stockholders equity; (xxxiv) capital expenditures; (xxxv) debt levels; (xxxvi) operating profit or net operating profit; (xxxvii) workforce diversity; (xxxviii) growth of net income or operating income; (xxxix) billings; (xl) bookings; (xli) employee retention; (xlii) initiation of phases of clinical trials and/or studies by specific dates; (xliii) acquisition of new customers, including institutional accounts; (xliv) customer retention and/or repeat order rate; (xlv) number of institutional customer accounts (xlvi) budget management; (xlvii) improvements in sample and test processing times; (xlviii) regulatory milestones; (xlix) progress of internal research or clinical programs; (l) progress of partnered programs; (li) partner satisfaction; (lii) milestones related to samples received and/or tests run; (liii) expansion of sales in additional geographies or markets; (liv) research progress, including the development of programs; (lv) submission to, or approval by, a regulatory body (including, but not limited to the U.S. Food and Drug Administration) of an applicable filing or a product; (lvi) timely completion of clinical trials; (lvii) milestones related to samples received and/or tests or panels run; (lviii) expansion of sales in additional geographies or markets; (lix) research progress, including the development of programs; (lx) patient samples processed and billed; (lxi) sample processing operating metrics (including, without limitation, failure rate maximums and reduction of repeat rates); (lxii) strategic partnerships or transactions (including in-licensing and out-licensing of intellectual property); (lxiii) pre-clinical development related to compound goals; (lxiv) customer satisfaction; and (lxv) and to the extent that an award is not intended to comply with Section 162(m) of the Code, other measures of performance selected by the board of directors of the combined company.

Performance goals may be based on a company-wide basis, with respect to one or more business units, divisions, affiliates or business segments, and in either absolute terms or relative to the performance of one or more comparable companies or the performance of one or more relevant indices. The compensation committee of the combined company s board of directors (or, to the extent that an award is not intended to qualify as performance-based compensation under Section 162(m) of the Code, the Plan Administrator) is authorized to make appropriate adjustments in the method of calculating the attainment of performance goals for a performance period as follows; *provided, however*, that to the extent that an award is intended to qualify as performance-based compensation under Section 162(m) of the Code, any such adjustment may be made only if such adjustment is objectively determinable and specified in the award agreement at the time the award is granted or in such other document setting forth the performance goals for the award at the time the performance goals are established: (i) to exclude restructuring and/or other nonrecurring charges; (ii) to exclude exchange rate effects; (iii) to exclude the effects of changes to U.S. GAAP; (iv) to exclude the effects of any statutory adjustments to corporate tax rates; (v) to exclude the effects of items that are unusual in nature or occur infrequently as determined under U.S. GAAP; (vi) to exclude the dilutive effects of acquisitions or joint ventures; (vii) to assume that any business divested by the combined company achieved performance objectives at targeted levels during the balance of a performance period following such divestiture; (viii) to exclude the effect of any change in the outstanding shares of common stock of the combined company by reason of any stock dividend or split, stock repurchase, reorganization, recapitalization, merger, consolidation, spin-off, combination or exchange of shares or other similar corporate change, or any distributions to common stockholders other than regular cash dividends; (ix) to exclude the effects of stock based compensation and the award of bonuses under the combined company s bonus plans; (x) to exclude costs incurred in connection with potential acquisitions or divestitures that are required to be expensed under U.S. GAAP; and (xi) to exclude the goodwill and intangible asset impairment charges that are required to be recorded under U.S. GAAP.

In addition, the compensation committee of the combined company s board of directors (or, to the extent that an award is not intended to qualify as performance-based compensation under Section 162(m) of the Code, the Plan Administrator) retains the discretion to reduce or eliminate the compensation or economic benefit due upon the attainment of any performance goals and to define the manner of calculating the performance criteria it selects to use for a performance period.

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Other Stock Awards

Other forms of stock awards valued in whole or in part by reference to, or otherwise based on, common stock may be granted either alone or in addition to other stock awards under the 2016 Plan. The Plan Administrator will have sole and complete authority to determine the persons to whom and the time or times at which such other stock awards will be granted, the number of shares of common stock to be granted and all other terms and conditions of such other stock awards.

Clawback Policy

Awards granted under the 2016 Plan will be subject to recoupment in accordance with any clawback policy that the combined company is required to adopt pursuant to the listing standards of any national securities exchange or association on which Signal s securities are listed or as is otherwise required by the Dodd-Frank Wall Street Reform and Consumer Protection Act or other applicable law. In addition, the Plan Administrator may impose other clawback, recovery or recoupment provisions in an award agreement as the Plan Administrator determines necessary or appropriate, including a reacquisition right in respect of previously acquired shares of common stock or other cash or property upon the occurrence of cause.

Changes to Capital Structure

In the event of certain capitalization adjustments, the Plan Administrator will appropriately adjust: (i) the class(es) and maximum number of securities subject to the 2016 Plan and by which the share reserve may increase automatically each year; (ii) the class(es) and maximum number of securities that may be issued pursuant to the exercise of ISOs; (iii) the class(es) and maximum number of securities that may be awarded to any participant pursuant to Section 162(m) limits; (iv) the class and maximum number of shares that may be awarded to any non-employee director; and (v) the class(es) and number of securities and price per share of stock subject to outstanding stock awards.

Corporate Transaction

In the event of a corporate transaction (as defined in the 2016 Plan and described below), the Plan Administrator may take one or more of the following actions with respect to stock awards, contingent upon the closing or consummation of the corporate transaction, unless otherwise provided in the instrument evidencing the stock award, in any other written agreement between the combined company or one of its affiliates and the participant or in Signal s director compensation policy, or unless otherwise provided by the Plan Administrator at the time of grant of the stock award:

arrange for the surviving or acquiring corporation (or its parent company) to assume or continue the stock award or to substitute a similar stock award for the stock award (including an award to acquire the same consideration paid to the combined company s stockholders pursuant to the corporate transaction);

arrange for the assignment of any reacquisition or repurchase rights held by the combined company in respect of common stock issued pursuant to the stock award to the surviving or acquiring corporation (or its parent company);

accelerate the vesting (and, if applicable, the exercisability) of the stock award to a date prior to the effective time of the corporate transaction as determined by the Plan Administrator (or, if the Plan Administrator does not determine such a date, to the date that is five days prior to the effective date of the corporate transaction), with the stock award terminating if not exercised (if applicable) at or prior to the effective time of the corporate transaction; *provided, however*, that the Plan Administrator may require participants to complete and deliver to Signal a notice of exercise before the effective date of a corporate transaction, which is contingent upon the effectiveness of the corporate transaction;

arrange for the lapse of any reacquisition or repurchase rights held by the combined company with respect to the stock award;

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cancel or arrange for the cancellation of the stock award, to the extent not vested or not exercised prior to the effective time of the corporate transaction, and pay such cash consideration (including no consideration) as the Plan Administrator may consider appropriate; and

cancel or arrange for the cancellation of the stock award, to the extent not vested or not exercised prior to the effective time of the corporate transaction, in exchange for a payment, in such form as may be determined by the combined company s board of directors equal to the excess, if any, of (i) the per share amount payable to holders of common stock in connection with the corporate transaction, over (ii) the per share exercise price under the applicable award. For clarity, this payment may be zero if the value of the property is equal to or less than the exercise price. In addition, any escrow, holdback, earnout or similar provisions in the definitive agreement for the corporate transaction may apply to such payment to the same extent and in the same manner as such provisions apply to the holders of common stock.

The Plan Administrator is not required to take the same action with respect to all stock awards or portions of stock awards or with respect to all participants. The Plan Administrator may take different actions with respect to the vested and unvested portions of a stock award.

In the event of a corporate transaction, unless otherwise provided in the instrument evidencing a performance cash award or any other written agreement between the combined company or one of its affiliates and the participant, or unless otherwise provided by the Plan Administrator, all performance cash awards will terminate prior to the effective time of the corporate transaction.

For purposes of the 2016 Plan, a corporate transaction generally will be deemed to occur in the event of the consummation of: (i) a sale or other disposition of all or substantially all of the combined company s consolidated assets; (ii) a sale or other disposition of more than 50% of Signal s outstanding securities; (iii) a merger, consolidation or similar transaction following which the combined company is not the surviving corporation; or (iv) a merger, consolidation or similar transaction following which the combined company is the surviving corporation but the shares of common stock outstanding immediately prior to the transaction are converted or exchanged into other property by virtue of the transaction.

Change in Control

Under the 2016 Plan, a stock award may be subject to additional acceleration of vesting and exercisability upon or after a change in control (as defined in the 2016 Plan and described below) as may be provided in the participant s stock award agreement, in any other written agreement with the combined company or one of its affiliates or in any director compensation policy, but in the absence of such provision, no such acceleration will occur.

For purposes of the 2016 Plan, a change in control generally will be deemed to occur in the event: (i) a person, entity or group acquires, directly or indirectly, Signal s securities representing more than 50% of the combined voting power of the combined company s then outstanding securities, other than by virtue of a merger, consolidation, or similar transaction; (ii) there is consummated a merger, consolidation, or similar transaction and, immediately after the consummation of such transaction, the combined company s stockholders immediately prior thereto do not own, directly or indirectly, more than 50% of the combined outstanding voting power of the surviving entity or the parent of the surviving entity in substantially the same proportions as their ownership of the combined company s outstanding voting securities immediately prior to such transaction; (iii) there is consummated a sale or other disposition of all or substantially all of the combined company s consolidated assets, other than a sale or other disposition to an entity in which more than 50% of the entity s combined voting power is owned by the combined company s stockholders in substantially the same proportions as their ownership of the combined company s outstanding voting securities

immediately prior to such sale or other disposition; or (iv) a majority of the combined company s board of directors becomes comprised of individuals whose nomination, appointment, or election was not approved by a majority of the board members or their approved successors.

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Plan Amendments and Termination

The Plan Administrator will have the authority to amend or terminate the 2016 Plan at any time. However, except as otherwise provided in the 2016 Plan or an award agreement, no amendment or termination of the 2016 Plan may materially impair a participant s rights under his or her outstanding awards without the participant s consent.

The combined company will obtain stockholder approval of any amendment to the 2016 Plan as required by applicable law and listing requirements. No incentive stock options may be granted under the 2016 Plan after the tenth anniversary of the date the 2016 Plan was adopted by Signal s board of directors.

U.S. Federal Income Tax Consequences

The following is a summary of the principal U.S. federal income tax consequences to participants and the combined company with respect to participation in the 2016 Plan, which will not become effective until the date of the closing of the Merger. No awards will be issued under the 2016 Plan prior to the date of the closing of the Merger. This summary is not intended to be exhaustive and does not discuss the income tax laws of any local, state or foreign jurisdiction in which a participant may reside. The information is based upon current federal income tax rules and therefore is subject to change when those rules change. Because the tax consequences to any participant may depend on his or her particular situation, each participant should consult the participant s tax adviser regarding the federal, state, local and other tax consequences of the grant or exercise of an award or the disposition of stock acquired the 2016 Plan. The 2016 Plan is not qualified under the provisions of Section 401(a) of the Code and is not subject to any of the provisions of the Employee Retirement Income Security Act of 1974. The combined company s ability to realize the benefit of any tax deductions described below depends on the combined company s generation of taxable income as well as the requirement of reasonableness, the provisions of Section 162(m) of the Code and the satisfaction of Signal s tax reporting obligations.

Nonstatutory Stock Options

Generally, there is no taxation upon the grant of a NSO if the stock option is granted with an exercise price equal to the fair market value of the underlying stock on the grant date. Upon exercise, a participant will recognize ordinary income equal to the excess, if any, of the fair market value of the underlying stock on the date of exercise of the stock option over the exercise price. If the participant is employed by the combined company or one of its affiliates, that income will be subject to withholding taxes. The participant s tax basis in those shares will be equal to their fair market value on the date of exercise of the stock option, and the participant s capital gain holding period for those shares will begin on that date.

Subject to the requirement of reasonableness, the provisions of Section 162(m) of the Code and the satisfaction of a tax reporting obligation, the combined company will generally be entitled to a tax deduction equal to the taxable ordinary income realized by the participant.

Incentive Stock Options

The 2016 Plan provides for the grant of stock options that are intended to qualify as incentive stock options, as defined in Section 422 of the Code. Under the Code, a participant generally is not subject to ordinary income tax upon the grant or exercise of an ISO. If the participant holds a share received upon exercise of an ISO for more than two years from the date the stock option was granted and more than one year from the date the stock option was exercised, which is referred to as the required holding period, the difference, if any, between the amount realized on a sale or other taxable disposition of that share and the participant s tax basis in that share will be long-term capital gain or loss.

If, however, a participant disposes of a share acquired upon exercise of an ISO before the end of the required holding period, which is referred to as a disqualifying disposition, the participant generally will recognize

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ordinary income in the year of the disqualifying disposition equal to the excess, if any, of the fair market value of the share on the date of exercise of the stock option over the exercise price. However, if the sales proceeds are less than the fair market value of the share on the date of exercise of the stock option, the amount of ordinary income recognized by the participant will not exceed the gain, if any, realized on the sale. If the amount realized on a disqualifying disposition exceeds the fair market value of the share on the date of exercise of the stock option, that excess will be short-term or long-term capital gain, depending on whether the holding period for the share exceeds one year.

For purposes of the alternative minimum tax, the amount by which the fair market value of a share of stock acquired upon exercise of an ISO exceeds the exercise price of the stock option generally will be an adjustment included in the participant s alternative minimum taxable income for the year in which the stock option is exercised. If, however, there is a disqualifying disposition of the share in the year in which the stock option is exercised, there will be no adjustment for alternative minimum tax purposes with respect to that share. In computing alternative minimum taxable income, the tax basis of a share acquired upon exercise of an ISO is increased by the amount of the adjustment taken into account with respect to that share for alternative minimum tax purposes in the year the stock option is exercised.

The combined company is not allowed a tax deduction with respect to the grant or exercise of an ISO or the disposition of a share acquired upon exercise of an ISO after the required holding period. If there is a disqualifying disposition of a share, however, the combined company will generally be entitled to a tax deduction equal to the taxable ordinary income realized by the participant, subject to the requirement of reasonableness and the provisions of Section 162(m) of the Code, and provided that either the employee includes that amount in income or the combined company timely satisfies its reporting requirements with respect to that amount.

Restricted Stock Awards

Generally, the recipient of a restricted stock award will recognize ordinary income at the time the stock is received equal to the excess, if any, of the fair market value of the stock received over any amount paid by the recipient in exchange for the stock. If, however, the stock is not vested when it is received (for example, if the employee is required to work for a period of time in order to have the right to sell the stock), the recipient generally will not recognize income until the stock becomes vested, at which time the recipient will recognize ordinary income equal to the excess, if any, of the fair market value of the stock on the date it becomes vested over any amount paid by the recipient in exchange for the stock. A recipient may, however, file an election with the Internal Revenue Service, within 30 days following his or her receipt of the stock award, to recognize ordinary income, as of the date the recipient receives the award, equal to the excess, if any, of the fair market value of the stock on the date the award is granted over any amount paid by the recipient for the stock.

The recipient s basis for the determination of gain or loss upon the subsequent disposition of shares acquired from a restricted stock award will be the amount paid for such shares plus any ordinary income recognized either when the stock is received or when the stock becomes vested.

Subject to the requirement of reasonableness, the provisions of Section 162(m) of the Code and the satisfaction of a tax reporting obligation, the combined company will generally be entitled to a tax deduction equal to the taxable ordinary income realized by the recipient of the restricted stock award.

Restricted Stock Unit Awards

Generally, the recipient of a restricted stock unit award structured to comply with the requirements of Section 409A of the Code or an exception to Section 409A of the Code will recognize ordinary income at the time the stock is delivered equal to the excess, if any, of the fair market value of the stock received over any amount paid by the recipient in exchange for the stock. To comply with the requirements of Section 409A of the Code, the stock subject to a restricted stock unit award may generally only be delivered upon one of the

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following events: a fixed calendar date (or dates), separation from service, death, disability or a change in control. If delivery occurs on another date, unless the restricted stock unit award otherwise complies with or qualifies for an exception to the requirements of Section 409A of the Code (including delivery upon achievement of a performance goal), in addition to the tax treatment described above, the recipient will owe an additional 20% federal tax and interest on any taxes owed.

The recipient s basis for the determination of gain or loss upon the subsequent disposition of shares acquired from a restricted stock unit award will be the amount paid for such shares plus any ordinary income recognized when the stock is delivered.

Subject to the requirement of reasonableness, the provisions of Section 162(m) of the Code and the satisfaction of a tax reporting obligation, the combined company will generally be entitled to a tax deduction equal to the taxable ordinary income realized by the recipient of the restricted stock unit award.

Stock Appreciation Rights

Generally, if a stock appreciation right is granted with an exercise price equal to the fair market value of the underlying stock on the grant date, the recipient will recognize ordinary income equal to the fair market value of the stock or cash received upon such exercise. Subject to the requirement of reasonableness, the provisions of Section 162(m) of the Code, and the satisfaction of a tax reporting obligation, the combined company will generally be entitled to a tax deduction equal to the taxable ordinary income realized by the recipient of the stock appreciation right.

New Plan Benefits

Awards granted under the 2016 Plan to Signal s executive officers and other employees are discretionary and are not subject to set benefits or amounts under the terms of the 2016 Plan. The 2016 Plan will not become effective until the closing of the Merger and neither Signal s board of directors nor Signal s compensation committee has granted any awards under the 2016 Plan subject to stockholder approval of this Signal Proposal No. 4. Accordingly, the benefits or amounts that will be received by or allocated to Signal s (or the combined company s) executive officers and other employees under the 2016 Plan, as well as the benefits or amounts which would have been received by or allocated to Signal s (or the combined company s) executive officers and other employees for fiscal year ended December 31, 2015 if the 2016 Plan had been in effect, are not determinable.

Required Vote

The affirmative vote of the holders of a majority of the shares of Signal common stock having voting power present in person or represented by proxy at the Signal special meeting is required to approve Signal Proposal No. 4. **Each of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9 are conditioned upon each other. Therefore, the Merger cannot be consummated without the approval of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9.**

Recommendation of Board of Directors

SIGNAL S BOARD OF DIRECTORS RECOMMENDS THAT SIGNAL STOCKHOLDERS VOTE FOR SIGNAL PROPOSAL NO. 4 TO APPROVE THE 2016 PLAN.

Signal Proposal No. 5: Approval of the Signal 2016 Employee Stock Purchase Plan

The board of directors of Signal has approved adoption of the Signal 2016 Employee Stock Purchase Plan, or the ESPP, subject to approval by Signal stockholders. In this Signal Proposal No. 5, Signal s board of directors is requesting stockholder approval of the ESPP.

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The discussion that follows is qualified in all respects to the terms of the ESPP. A copy of the ESPP is attached as *Annex C* to this proxy statement/prospectus/information statement. Signal stockholders should refer to the ESPP for more complete and detailed information about the terms and conditions of the ESPP.

If this Signal Proposal No. 5 is approved by Signal stockholders, the ESPP will become effective as of the date of the closing of the Merger. In the event that Signal stockholders do not approve this proposal, the ESPP will not become effective. Signal does not maintain any other employee stock purchase plans. Approval of the ESPP by Signal stockholders will allow the combined company to provide its employees with the opportunity to acquire an ownership interest in the combined company through their participation in the ESPP, thereby encouraging them to remain in service and more closely aligning their interests with those of the combined company s stockholders.

Description of the ESPP

The material features of the ESPP are described below. The following description of the ESPP is a summary only and is qualified in its entirety by reference to the text of the ESPP.

Purpose

The purpose of the ESPP is to provide a means by which the combined company s employees may be given an opportunity to purchase shares of common stock following the closing of the Merger, to assist the combined company in retaining the services of its employees, to secure and retain the services of new employees and to provide incentives for such persons to exert maximum efforts for Signal s success. The rights to purchase common stock granted under the ESPP are intended to qualify as options issued under an employee stock purchase plan as that term is defined in Section 423(b) of the Code.

Administration

The combined company s board of directors will have the power to administer the ESPP and may also delegate administration of the ESPP to a committee comprised of one or more members of its board of directors. The combined company s board of directors will delegate concurrent authority to administer the 2016 Plan to its compensation committee, but may, at any time, revest in itself some or all of the power delegated to its compensation committee. The combined company s board of directors and its compensation committee will each be considered to be a Plan Administrator for purposes of this proposal. The Plan Administrator has the final power to construe and interpret both the ESPP and the rights granted under it. The Plan Administrator has the power, subject to the provisions of the ESPP, to determine when and how rights to purchase common stock will be granted, the provisions of each offering of such rights (which need not be identical), and whether employees of any parent or subsidiary companies will be eligible to participate in the ESPP.

Stock Subject to ESPP

Subject to adjustment for specified changes in Signal s capitalization and for the reverse stock split, the maximum number of shares of common stock that may be issued under the ESPP is 210,162 shares, plus the number of shares of common stock that are automatically added on January 1st of each year for a period of up to ten years, commencing on January 1 following the effective date of the ESPP and ending on (and including) January 1, 2026, in an amount equal to the lesser of (i) 1% of the total number of shares of Signal s common stock outstanding on December 31st of the preceding calendar year, and (ii) 367,784 shares of common stock; provided, that prior to the date of any annual increase, the board of directors of the combined company may determine that such increase will be less than the amount set forth in clauses (i) or (ii). If any rights granted under the ESPP terminate without being exercised in full,

the shares of common stock not purchased under such rights again become available for issuance under the ESPP. The shares of common stock issuable under the ESPP will be shares of authorized but unissued or reacquired common stock, including shares repurchased by Signal on the open market.

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Offerings

The ESPP will be implemented by offerings of rights to purchase common stock to all eligible employees. The Plan Administrator will determine the duration of each offering period, provided that in no event may an offering period exceed 27 months. The Plan Administrator may establish separate offerings which vary in terms (although not inconsistent with the provisions of the ESPP or the requirements of applicable laws). Each offering period will have one or more purchase dates, as determined by the Plan Administrator prior to the commencement of the offering period. The Plan Administrator has the authority to alter the terms of an offering prior to the commencement of the offering period, including the duration of subsequent offering periods. When an eligible employee elects to join an offering period, he or she is granted a right to purchase shares of common stock on each purchase date within the offering period. On the purchase date, all contributions collected from the participant are automatically applied to the purchase of Signal s common stock, subject to certain limitations (which are described further below under *Eligibility*).

The Plan Administrator has the discretion to structure an offering so that if the fair market value of a share of common stock on any purchase date during the offering period is less than or equal to the fair market value of a share of common stock on the first day of the offering period, then that offering will terminate immediately following the purchase of shares of common stock on such purchase date, and the participants in such terminated offering will be automatically enrolled in a new offering that begins immediately after such purchase date.

Eligibility

Any individual who is employed by the combined company (or by any of its parent or subsidiary companies if such company is designated by the Plan Administrator as eligible to participate in the ESPP) may participate in offerings under the ESPP, provided such individual has been employed by the combined company (or its parent or subsidiary, if applicable) for such continuous period preceding the first day of the offering period as the Plan Administrator may require, but in no event may the required period of continuous employment be equal to or greater than two years. In addition, the Plan Administrator may provide that an employee will not be eligible to be granted purchase rights under the ESPP unless such employee is customarily employed for more than 20 hours per week and five months per calendar year. The Plan Administrator may also provide in any offering that certain of the combined company s employees who are highly compensated as defined in the Code are not eligible to participate in the ESPP.

No employee will be eligible to participate in the ESPP if, immediately after the grant of purchase rights, the employee would own, directly or indirectly, stock possessing 5% or more of the total combined voting power or value of all classes of Signal s stock or of any of Signal s parent or subsidiary companies, including any stock which such employee may purchase under all outstanding purchase rights and options. In addition, no employee may purchase more than $25,000 worth of Signal s common stock (determined based on the fair market value of the shares at the time such rights are granted) under all Signal s employee stock purchase plans and any employee stock purchase plans of the combined company s parent or subsidiary companies for each calendar year during which such rights are outstanding.

Participation in the ESPP

An eligible employee may enroll in the ESPP by delivering, prior to the date selected by the Plan Administrator as the beginning of an offering period, an agreement authorizing contributions which may not exceed the maximum amount specified by the Plan Administrator, but in any case which may not exceed 15% of such employee s earnings during the offering period. Each participant will be granted a separate purchase right for each offering in which he or she participates. Unless an employee s participation is discontinued, his or her purchase right will be exercised automatically at the end of each purchase period at the applicable purchase price.

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Purchase Price

The purchase price per share at which shares of common stock are sold on each purchase date during an offering period will not be less than the lower of (i) 85% of the fair market value of a share of common stock on the first day of the offering period or (ii) 85% of the fair market value of a share of common stock on the purchase date. As of January 5, 2017, the closing price of Signal s common stock as reported on The NASDAQ Capital Market was $5.33 per share.

Payment of Purchase Price; Payroll Deductions

The purchase of shares during an offering period generally will be funded by a participant s payroll deductions accumulated during the offering period. A participant may change his or her rate of contributions, as determined by the Plan Administrator in the offering. All contributions made for a participant are credited to his or her account under the ESPP and deposited with the combined company s general funds.

Purchase Limits

In connection with each offering made under the ESPP, the Plan Administrator may specify (i) a maximum number of shares of common stock that may be purchased by any participant pursuant to such offering, (ii) a maximum number of shares of common stock that may be purchased by any participant on any purchase date pursuant to such offering, (iii) a maximum aggregate number of shares of common stock that may be purchased by all participants pursuant to such offering, and/or (iv) a maximum aggregate number of shares of common stock that may be purchased by all participants on any purchase date pursuant to such offering. If the aggregate purchase of shares of common stock issuable upon exercise of purchase rights granted under such offering would exceed any such maximum aggregate number, then the Plan Administrator will make a pro rata allocation of available shares in a uniform and equitable manner.

Withdrawal

Participants may withdraw from an offering by delivering a withdrawal form to the combined company and terminating their contributions. Such withdrawal may be elected at any time prior to the end of an offering, except as otherwise provided by the Plan Administrator. Upon such withdrawal, the combined company will distribute to the employee his or her accumulated but unused contributions without interest, and such employee s right to participate in that offering will terminate. However, an employee s withdrawal from an offering does not affect such employee s eligibility to participate in any other offerings under the ESPP.

Termination of Employment

A participant s rights under any offering under the ESPP will terminate immediately if the participant either (i) is no longer employed by the combined company or any of its parent or subsidiary companies (subject to any post-employment participation period required by law) or (ii) is otherwise no longer eligible to participate. In such event, the combined company will distribute to the participant his or her accumulated but unused contributions without interest.

Restrictions on Transfer

Rights granted under the ESPP are not transferable except by will, by the laws of descent and distribution, or if permitted by the combined company, by a beneficiary designation. During a participant s lifetime, such rights may

only be exercised by the participant.

Changes in Capitalization

In the event of certain changes in the combined company s capitalization, the Plan Administrator will appropriately adjust: (i) the class(es) and maximum number of securities subject to the ESPP; (ii) the class(es)

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and maximum number of securities by which the share reserve it to increase automatically each year; (iii) the class(es) and number of securities subject to, and the purchase price applicable to, outstanding offerings and purchase rights; and (iv) the class(es) and number of securities that are the subject of any purchase limits under each ongoing offering.

Effect of Certain Corporate Transactions

In the event of a corporate transaction (as defined in the ESPP and described below), (i) any surviving or acquiring corporation (or its parent company) may assume or continue outstanding purchase rights granted under the ESPP or may substitute similar rights (including a right to acquire the same consideration paid to the stockholders in the corporate transaction) for such outstanding purchase rights, or (ii) if any surviving or acquiring corporation (or its parent company) does not assume or continue such outstanding purchase rights or does not substitute similar rights for such outstanding purchase rights, then the participants accumulated contributions will be used to purchase shares of common stock within ten business days prior to the corporate transaction under such purchase rights, and such purchase rights will terminate immediately after such purchase.

For purposes of the ESPP, a corporate transaction generally will be deemed to occur in the event of the consummation of: (i) a sale or other disposition of all or substantially all of the combined company s consolidated assets; (ii) a sale or other disposition of at least 50% of the combined company s outstanding securities; (iii) a merger, consolidation or similar transaction following which the combined company is not the surviving corporation; or (iv) a merger, consolidation or similar transaction following which the combined company is the surviving corporation but the shares of its common stock outstanding immediately prior to such transaction are converted or exchanged into other property by virtue of such transaction.

Duration, Amendment and Termination

The Plan Administrator may amend or terminate the ESPP at any time. However, except in regard to certain capitalization adjustments, any such amendment must be approved by the combined company s stockholders if such approval is required by applicable law or listing requirements.

Any outstanding purchase rights granted before an amendment or termination of the ESPP will not be materially impaired by any such amendment or termination, except (i) with the consent of the employee to whom such purchase rights were granted, (ii) as necessary to comply with applicable laws, listing requirements or governmental regulations (including Section 423 of the Code), or (iii) as necessary to obtain or maintain favorable tax, listing or regulatory treatment.

Notwithstanding anything in the ESPP or any offering to the contrary, the Plan Administrator will be entitled to: (i) establish the Exchange Ratio applicable to amounts withheld in a currency other than U.S. dollars; (ii) permit contributions in excess of the amount designated by a participant in order to adjust for mistakes in the processing of properly completed contribution elections; (iii) establish reasonable waiting and adjustment periods and/or accounting and crediting procedures to ensure that amounts applied toward the purchase of common stock for each participant properly correspond with amounts withheld from the participant s contributions; (iv) amend any outstanding purchase rights or clarify any ambiguities regarding the terms of any offering to enable such purchase rights to qualify under and/or comply with Section 423 of the Code; and (v) establish other limitations or procedures as the Plan Administrator determines in its sole discretion advisable that are consistent with the ESPP. Any such actions by the Plan Administrator will not be considered to alter or impair any purchase rights granted under an offering as they are part of the initial terms of each offering and the purchase rights granted under each offering.

Federal Income Tax Information

The following is a summary of the principal U.S. federal income tax consequences to participants and the combined company with respect to participation in the ESPP. This summary is not intended to be exhaustive and

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does not discuss the income tax laws of any local, state or foreign jurisdiction in which a participant may reside. The information is based upon current federal income tax rules and therefore is subject to change when those rules change. Because the tax consequences to any participant may depend on his or her particular situation, each participant should consult the participant s tax adviser regarding the federal, state, local, and other tax consequences of the grant or exercise of a purchase right or the sale or other disposition of common stock acquired under the ESPP. The ESPP is not qualified under the provisions of Section 401(a) of the Code and is not subject to any of the provisions of the Employee Retirement Income Security Act of 1974, as amended.

Rights granted under the ESPP are intended to qualify for favorable federal income tax treatment associated with rights granted under an employee stock purchase plan which qualifies under the provisions of Section 423 of the Code.

A participant will be taxed on amounts withheld for the purchase of shares of common stock as if such amounts were actually received. Otherwise, no income will be taxable to a participant as a result of the granting or exercise of a purchase right until a sale or other disposition of the acquired shares. The taxation upon such sale or other disposition will depend upon the holding period of the acquired shares.

If the shares are sold or otherwise disposed of more than two years after the beginning of the offering period and more than one year after the shares are transferred to the participant, then the lesser of the following will be treated as ordinary income: (i) the excess of the fair market value of the shares at the time of such sale or other disposition over the purchase price; or (ii) the excess of the fair market value of the shares as of the beginning of the offering period over the purchase price (determined as of the beginning of the offering period). Any further gain or any loss will be taxed as a long-term capital gain or loss.

If the shares are sold or otherwise disposed of before the expiration of either of the holding periods described above, then the excess of the fair market value of the shares on the purchase date over the purchase price will be treated as ordinary income at the time of such sale or other disposition. The balance of any gain will be treated as capital gain. Even if the shares are later sold or otherwise disposed of for less than their fair market value on the purchase date, the same amount of ordinary income is attributed to the participant, and a capital loss is recognized equal to the difference between the sales price and the fair market value of the shares on such purchase date. Any capital gain or loss will be short-term or long-term, depending on how long the shares have been held.

There are no federal income tax consequences to the combined company by reason of the grant or exercise of rights under the ESPP. The combined company is entitled to a deduction to the extent amounts are taxed as ordinary income to a participant for shares sold or otherwise disposed of before the expiration of the holding periods described above (subject to the requirement of reasonableness and the satisfaction of tax reporting obligations).

New Plan Benefits

Participation in the ESPP is voluntary and each eligible employee will make his or her own decision regarding whether and to what extent to participate in the ESPP. In addition, Signal s board of directors and Signal s compensation committee have not granted any purchase rights under the ESPP that are subject to stockholder approval of this proposal. The ESPP will not become effective until the date of the closing of the Merger. Accordingly, the benefits or amounts that will be received by or allocated to Signal s (or the combined company s) executive officers and other employees under the ESPP, as well as the benefits or amounts which would have been received by or allocated to Signal s (or the combined company s) executive officers and other employees for the fiscal year ended December 31, 2015 if the ESPP had been in effect, are not determinable. No non-employee directors will be eligible to participate in the ESPP.

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Required Vote

The affirmative vote of the holders of a majority of the shares of Signal common stock having voting power present in person or represented by proxy at the Signal special meeting is required to approve Signal Proposal No. 5. **Each of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9 are conditioned upon each other. Therefore, the Merger cannot be consummated without the approval of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9.**

Recommendation of Board of Directors

SIGNAL S BOARD OF DIRECTORS RECOMMENDS THAT SIGNAL STOCKHOLDERS VOTE FOR SIGNAL PROPOSAL NO. 5 TO APPROVE THE ESPP.

Signal Proposal No. 6: Approval of Name Change

At the Signal special meeting, holders of Signal common stock will be asked to approve the amendment to the certificate of incorporation of Signal to change the name of the corporation from Signal Genetics, Inc. to Miragen Therapeutics, Inc. by filing an amendment to the certificate of incorporation at the effective time of the Merger. A copy of the proposed amendment to Signal s certificate of incorporation is attached as *Annex D* to this proxy statement/prospectus/information statement. The primary reason for the corporate name change is that management believes this will allow for brand recognition of Miragen product candidates and product candidate pipeline following the consummation of the Merger. Signal management believes that the current name will no longer accurately reflect the business of Signal and the mission of Signal subsequent to the consummation of the Merger.

Required Vote

The affirmative vote of holders of a majority of the outstanding shares of Signal common stock entitled to vote on the record date for the Signal special meeting is required to approve Signal Proposal No. 6. **Each of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9 are conditioned upon each other. Therefore, the Merger cannot be consummated without the approval of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9.**

Recommendation of Board of Directors

SIGNAL S BOARD OF DIRECTORS RECOMMENDS THAT SIGNAL STOCKHOLDERS VOTE FOR SIGNAL PROPOSAL NO. 6 TO APPROVE THE NAME CHANGE.

Signal Proposal No. 7: Approval of the Amendment to the Certificate of Incorporation of Signal Effecting the Reverse Stock Split.

General

At the Signal special meeting, Signal stockholders will be asked to approve an amendment to its certificate of incorporation effecting the reverse stock split of all issued and outstanding shares of Signal common stock, which will reduce the number of shares of outstanding Signal common stock in accordance with a ratio to be determined by Signal s board of directors within a range of one new share for every one to 15 shares of outstanding Signal common stock (or any number in between). A copy of the proposed amendment to Signal s certificate of incorporation is attached as *Annex E* to this proxy statement/prospectus/information statement. This proposal is referred to as the reverse stock split proposal. Signal s board of directors has declared such proposed amendment to be advisable and has unanimously recommended that this proposed amendment be presented to Signal stockholders for approval.

Assuming the stockholders approve the proposal, Signal s board of directors will have the sole discretion under Section 242(c) of the General Corporation Law of the State of Delaware as it determines to be in the best interest

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of Signal and its stockholders, both to select the specific exchange ratio within the designated range of one to 15 (or any number in between) and also to decide whether or not to proceed to effect a reverse stock split or instead to abandon the proposed certificate of amendment altogether. If a certificate of amendment is filed with the Secretary of State of the State of Delaware, the certificate of amendment to the certificate of incorporation will affect the reverse stock split by reducing the outstanding number of shares of the Signal common stock by the ratio to be determined by Signal s board of directors, but will not increase the par value of the Signal common stock, and will not change the number of authorized shares of Signal common stock. Signal s board of directors decision to effect a reverse stock split is based on a number of factors, including market conditions, existing and expected trading prices for Signal common stock and the applicable listing requirements of The NASDAQ Capital Market.

Upon the effectiveness of the proposed amendment effecting the reverse stock split, or the reverse split effective time, every one to 15 shares (or any number in between) of Signal common stock outstanding immediately prior to the reverse split effective time will be combined and reclassified into one share of Signal common stock. The actions taken in connection with the reverse stock split will reduce the number of outstanding shares of Signal common stock.

Purpose

Signal s board of directors believes that a reverse stock split is desirable for the following reasons:

- the board of directors believes effecting the reverse stock split may be an effective means of maintaining the compliance with the listing requirements of The NASDAQ Capital Market in the future; and

- the board of directors believes that a higher stock price may help generate investor interest in Signal s common stock.

Signal s common stock is currently listed on The NASDAQ Capital Market. Signal has filed an initial listing application with NASDAQ to seek listing for the combined company on The NASDAQ Capital Market upon the closing of the Merger. According to the applicable rules and regulations of The NASDAQ Stock Market LLC, an issuer must apply for initial listing following a transaction in which the issuer combines with a non-NASDAQ listed entity, resulting in a change of control of the issuer and potentially allowing the non-NASDAQ listed entity to obtain a NASDAQ listing. Furthermore, the listing standards of The NASDAQ Capital Market will require Signal to have, among other things, a $4.00 per share minimum bid price upon the closing of the Merger. Signal s board of directors expects that a reverse stock split of Signal common stock will increase the market price of Signal common stock so that Signal is able to maintain compliance with the relevant listing requirements of The NASDAQ Capital Market upon completion of the Merger.

On January 5, 2017, the closing price of Signal common stock was $5.33 per share. Signal s board of directors also believes that an increase in the market price of Signal common stock expected as a result of implementing a reverse stock split will improve the marketability and liquidity of Signal common stock and will encourage interest and trading in Signal common stock. Because of the trading volatility often associated with low-priced stocks, many brokerage houses and institutional investors have internal policies and practices that either prohibit them from investing in low-priced stocks or tend to discourage individual brokers from recommending low-priced stocks to their customers. Some of those policies and practices may function to make the processing of trades in low-priced stocks economically unattractive to brokers. Moreover, investors may also be dissuaded from purchasing lower priced stock because the brokerage commissions, as a percentage of the total transaction, tend to be higher. Signal s board of directors believes that the anticipated higher market price expected to result from a reverse stock split will reduce, to

some extent, the negative effects of the policies and practices of institutional investors and brokerage houses described above on the liquidity and marketability of Signal common stock.

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Signal cannot predict whether the reverse stock split will increase the market price of Signal common stock. Furthermore, there can be no assurance that: (i) the market price per share following the reverse stock split would rise in proportion to the reduction in the number of shares of Signal common stock outstanding due to the reverse stock split; (ii) the market price per share following the reverse stock split would meet the minimum bid price required for continued listing on The NASDAQ Capital Market or, if met, that the price would remain above the minimum for a sustained period of time; (iii) Signal would otherwise meet the requirements of The NASDAQ Stock Market LLC for listing on The NASDAQ Capital Market even if the per share market price of Signal common stock after the reverse stock split meets the required minimum price; (iv) the reverse stock split would result in a per share price that would attract brokers and investors who do not trade in lower-priced stock; and (v) the liquidity of Signal common stock would not be harmed by the reduced number of shares outstanding after the reverse stock split.

The market price of Signal common stock will also be based on Signal s performance and other factors, some of which are unrelated to the number of shares outstanding. If the reverse stock split is effected and the market price of Signal common stock declines, the percentage decline as an absolute number and as a percentage of Signal overall market capitalization may be greater than would occur in the absence of the proposed reverse stock split.

Signal s Discretion to Effect the Reverse Stock Split

If the reverse stock split proposal is approved by the Signal stockholders, the proposed amendment will be effected, if at all, only upon a determination by Signal s board of directors that a reverse stock split within a range of one for every one to 15 shares of Signal common stock (or any number in between) remains in the best interests of Signal and its stockholders based on the factors described above. Notwithstanding stockholders approval of the reverse stock split proposal, Signal s board of directors may, in its sole discretion, abandon the proposed amendment and determine prior to the effectiveness of any filing with the Secretary of State of the State of Delaware not to effect the reverse stock split of Signal common stock, as permitted under Section 242(c) of the DGCL.

Principal Effects of the Reverse Stock Split

The proposed form of amendment to the certificate of incorporation of Signal effecting the reverse stock split is set forth in *Annex E* to this proxy statement/prospectus/information statement.

If the reverse stock split is effected, it will be effected simultaneously for all outstanding shares of Signal common stock and the reverse stock split ratio will be the same for all shares of Signal common stock. The reverse stock split will affect all of Signal stockholders uniformly and will not affect any stockholder s percentage ownership interests in Signal, except to the extent that the reverse stock split results in any of Signal stockholders owning a fractional share. Common stock combined pursuant to the reverse stock split will remain fully paid and nonassessable. The number of stockholders of record will not be affected by the proposed reverse stock split (except to the extent that any stockholder holds only a fractional share interest after the application of the reverse stock split and receives cash for such interest). The reverse stock split will not affect the number of authorized shares of Signal common stock, which will continue to be authorized pursuant to the certificate of incorporation of Signal. Because the number of authorized shares of common stock will not be proportionally reduced by the reverse stock split, one of the effects of the reverse stock split will be to effectively increase the proportion of authorized shares that are unissued relative to those that are issued. This could result in Signal s management being able to issue more shares without further stockholder approval, unless required by applicable law.

The table below sets forth the anticipated effects of the reverse stock split at various reverse split ratios and Exchange Ratios. The number of shares in the table below are approximated, do not reflect the fractional shares that will result from the reverse stock split and assumes that Miragen s shares will be converted at various Exchange Ratios based on

the reverse split ratio, which gives effect to the reverse stock split and is estimated as

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of December 31, 2016, and assumes the issuance of shares of Miragen common stock in the concurrent financing.

	Number of shares outstanding after the Merger	Number of shares reserved under the terms of all convertible securities(1)	Number of authorized shares that will be available and unreserved(2)
With no reverse stock split	21,177,498	4,438,745	24,383,757
After 2-for-1 reverse stock split(3)	10,588,729	2,219,372	37,191,899
After 3-for-1 reverse stock split	7,509,146	1,479,581	41,011,273
After 4-for-1 reverse stock split	5,294,334	1,109,687	43,595,979
After 5-for-1 reverse stock split	4,235,439	887,748	44,876,813
After 6-for-1 reverse stock split	3,529,543	739,791	45,730,666
After 7-for-1 reverse stock split	3,025,316	634,105	46,340,579
After 8-for-1 reverse stock split	2,647,126	554,842	46,798,032
After 9-for-1 reverse stock split	2,353,008	493,192	47,153,800
After 10-for-1 reverse stock split	2,117,710	443,873	47,438,417
After 11-for-1 reverse stock split	1,925,194	403,523	47,671,283
After 12-for-1 reverse stock split	1,764,732	369,895	47,865,373
After 13-for-1 reverse stock split	1,629,026	341,441	48,029,533
After 14-for-1 reverse stock split	1,512,639	317,053	48,170,308
After 15-for-1 reverse stock split	1,411,793	295,916	48,292,291

(1) This column includes any shares of common stock reserved for issuance under (i) outstanding options issued under the Miragen 2008 Plan as of December 31, 2016, (ii) outstanding warrants of Miragen to be assumed by Signal in connection with the Merger as of December 31, 2016, (iii) outstanding warrants of Signal as of December 31, 2016, (iv) the 2016 Plan and (v) the ESPP.

(2) The number of authorized shares of Signal common stock that will be available and unreserved immediately following the reverse stock split effective time assumes that the authorized number of shares of Signal s common stock is 50,000,000 and does not give effect to the proposed increase of the authorized number of shares of Signal common stock under Signal Proposal No. 8. After giving effect to this proposed increase to the authorized number of shares of Signal common stock to 100,000,000 under Signal Proposal No. 8, the number of authorized shares of Signal common stock that will be available and unreserved immediately following the reverse stock split effective time would be between 74,383,757 and 98,292,291.

(3) Provided to illustrate the potential range of shares in the event the reverse split ratio is determined to be a number between 1-for-1 and 2-for-1.

Signal has no current plans, arrangements or understandings to issue shares that will be available and unreserved after the completion of the Merger and the other transactions described in this proxy statement/prospectus/information statement, other than in connection with the Merger and to satisfy obligations under the combined company s warrants and employee stock options from time to time as such warrants and options are exercised.

Signal will continue to be subject to the periodic reporting requirements of the Exchange Act after the reverse stock split. Signal common stock will continue to be listed on The NASDAQ Capital Market under the symbol SGNL. After completion of the Merger, Signal expects to trade on The NASDAQ Capital Market under the symbol MGEN.

Procedure for Effecting Reverse Stock Split and Exchange of Stock Certificates

If the certificate of amendment is approved by Signal stockholders, and if Signal still believes that a reverse stock split is in the best interests of Signal and its stockholders, Signal will file the certificate of amendment with the Secretary of State of the State of Delaware at such time as Signal may determine to be the appropriate effective time for the reverse stock split. The reverse split would become effective at immediately upon filing of the

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certificate of amendment on the date of filing of the certificate of amendment. Signal may delay effecting the reverse stock split without resoliciting stockholder approval.

Beginning at the reverse split effective time, each certificate representing pre-split shares will be deemed for all corporate purposes to evidence ownership of post-split shares. Except as explained below with respect to fractional shares, at the reverse split effective time, shares of Signal common stock issued and outstanding immediately prior to the reverse split effective time will be combined and reclassified, automatically and without any action on the part of the stockholders, into a lesser number of new shares of Signal common stock in accordance with the reverse stock split ratio within a range of one to 15 shares of Signal common stock (or any number in between) for every one outstanding share of Signal common stock.

As soon as practicable after the effective date of the reverse split, Signal stockholders will be notified that the reverse stock split has been effected. Signal expects that its transfer agent will act as exchange agent for purposes of implementing the exchange of stock certificates. Holders of pre-split shares will be asked to surrender to the exchange agent certificates representing their pre-split shares in exchange for certificates representing post-split shares in accordance with the procedures to be set forth in a letter of transmittal to be sent by Signal. No new certificates will be issued to a stockholder until such stockholder has surrendered such stockholder s outstanding certificate(s) together with the properly completed and executed letter of transmittal to the exchange agent. Any pre-split shares submitted for transfer, whether pursuant to a sale or other disposition, or otherwise, will automatically be exchanged for post-split shares.

SIGNAL STOCKHOLDERS SHOULD NOT DESTROY ANY STOCK CERTIFICATE(S) AND SHOULD NOT SUBMIT ANY CERTIFICATE(S) UNTIL REQUESTED TO DO SO.

Fractional Shares

No fractional shares will be issued in connection with the reverse stock split. Signal stockholders of record who otherwise would be entitled to receive fractional shares because they hold a number of pre-split shares not evenly divisible by the number of pre-split shares for which each post-split share is to be exchanged will be entitled, upon surrender to the exchange agent of certificates representing such shares, to a cash payment in lieu thereof at a price equal to the fraction to which the stockholder would otherwise be entitled multiplied by the closing price of the common stock on The NASDAQ Capital Market on the last trading day prior to the effective date of the reverse split or, if such price is not available, the average of the last bid and asked prices of the common stock on such day or other price determined by Signal s board of directors. The ownership of a fractional share will not give the holder thereof any voting, dividend or other rights except to receive payment therefor as described herein.

Stockholders should be aware that, under the escheat laws of the various jurisdictions where stockholders reside, where Signal is domiciled, and where the funds will be deposited, sums due for fractional interests that are not timely claimed after the effective date of the split may be required to be paid to the designated agent for each such jurisdiction, unless correspondence has been received by Signal or the exchange agent concerning ownership of such funds within the time permitted in such jurisdiction. Thereafter, stockholders otherwise entitled to receive such funds will have to seek to obtain them directly from the state to which they were paid.

Accounting Consequences

The par value per share of Signal common stock will remain unchanged at $0.01 per share after the reverse stock split. As a result, at the effective time of the reverse split, the stated capital on Signal s balance sheet attributable to Signal common stock will be reduced proportionately based on the reverse stock split ratio, from its present amount, and the

additional paid-in capital account will be increased for the amount by which the stated capital is reduced. After the reverse stock split (and disregarding the impact of shares of Signal common stock issued in the Merger), net income or loss per share, and other per share amounts will be increased because there will be fewer shares of Signal common stock outstanding. In future financial statements, net income or loss per share

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and other per share amounts for periods ending before the reverse stock split will be recast to give retroactive effect to the reverse stock split.

Potential Anti-Takeover Effect

Although the increased proportion of unissued authorized shares to issued shares could, under certain circumstances, have an anti-takeover effect (for example, by permitting issuances that would dilute the stock ownership of a person seeking to effect a change in the composition of Signal s board of directors or contemplating a tender offer or other transaction for the combination of Signal with another company), the reverse stock split proposal is not being proposed in response to any effort of which Signal is aware to accumulate shares of Signal common stock or obtain control of Signal, nor is it part of a plan by management to recommend a series of similar amendments to Signal s board of directors and stockholders, other than to complete the Merger with Miragen. Other than the reverse stock split proposal and the other proposals set forth in this proxy statement/prospectus/information statement pertaining to the Merger, Signal s board of directors does not currently contemplate recommending the adoption of any other actions that could be construed to affect the ability of third parties to take over or change control of Signal.

No Appraisal Rights

Under the DGCL, Signal stockholders are not entitled to appraisal rights with respect to the reverse stock split, and Signal will not independently provide stockholders with any such right.

Material U.S. Federal Income Tax Consequences of the Reverse Stock Split

In the opinion of Pillsbury, counsel to Signal, and Cooley, counsel to Miragen, the following is a discussion of material U.S. federal income tax consequences of the reverse stock split to holders of Signal common stock. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local, or foreign tax laws are not discussed. This discussion is based on the Code, U.S. Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the IRS each as in effect as of the date of the Merger. These authorities are subject to differing interpretations or change. Any such change, which may or may not be retroactive, could alter the tax consequences to holders of Signal common stock.

This discussion does not address all U.S. federal income tax consequences relevant to the particular circumstances of a Signal common stockholder. In addition, it does not address consequences relevant to holders of Signal common stock that are subject to particular rules, including, without limitation:

- persons who hold their Signal common stock in a functional currency other than the U.S. dollar;
- persons who hold Signal common stock that constitutes qualified small business stock under Section 1202 of the Code or as Section 1244 stock for purposes of Section 1244 of the Code;
- persons holding Signal common stock as part of an integrated investment (including a straddle, pledge against currency risk, constructive sale or conversion transaction or other integrated or risk reduction transactions) consisting of shares of Signal common stock and one or more other positions;

persons who are not U.S. Holders as defined below;

banks, insurance companies, mutual funds, tax-exempt entities, financial institutions, broker-dealers;

real estate investment trusts or regulated investment companies;

persons who do not hold their Signal common stock as a capital asset within the meaning of Section 1221 of the Code;

partnerships or other entities classified as partnerships or disregarded entities for U.S. federal income tax purposes, S corporations or other pass-through entities (including hybrid entities);

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persons who acquired their Signal common stock pursuant to the exercise of compensatory options or in other compensatory transactions;

persons who acquired their Signal common stock pursuant to the exercise of warrants or conversion rights under convertible instruments;

persons who acquired their Signal common stock in a transaction subject to the gain rollover provisions of Section 1045 of the Code; and

persons who hold their Signal common stock through individual retirement accounts or other tax-deferred accounts.

This discussion is limited to holders of Signal common stock that are U.S. Holders. For purposes of this discussion, a U.S. Holder is a beneficial owner of Signal common stock that, for U.S. federal income tax purposes, is or is treated as:

an individual who is a citizen or resident of the United States;

a corporation (or other entity taxable as a corporation for U.S. federal income tax purposes) created or organized in or 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 taxation regardless of its source; or

a trust if either (i) a court within the United States is able to exercise primary supervision over the administration of such trust and one or more United States persons (within the meaning of Section 7701(a)(30) of the Code) are authorized or have the authority to control all substantial decisions of such trust, or (ii) the trust was in existence on August 20, 1996 and has a valid election in effect under applicable Treasury Regulations to be treated as a United States person for U.S. federal income tax purposes.

If an entity treated as a partnership for U.S. federal income tax purposes holds Signal 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. If you are a partnership or a partner of a partnership you should consult your tax advisor regarding the tax consequences to you.

In addition, the following discussion does not address (i) any U.S. federal non-income tax consequences of the reverse stock split, including estate, gift or other tax consequences, (ii) any state, local or non-U.S. tax law consequences of the reverse stock split, (iii) the Medicare contribution tax on net investment income or the alternative minimum tax, (iv) the tax consequences of transactions effectuated before, after or at the same time as the reverse stock split (whether or not they are in connection with the reverse stock split), and (v) the tax consequences to holders of options, warrants or similar rights to purchase Signal common stock.

IN LIGHT OF THE FOREGOING HOLDERS OF SIGNAL COMMON STOCK SHOULD CONSULT THEIR OWN TAX ADVISORS REGARDING THE TAX CONSEQUENCES TO THEM OF THE REVERSE STOCK SPLIT, INCLUDING THE APPLICABLE U.S. FEDERAL, STATE, LOCAL AND NON-U.S. INCOME AND OTHER TAX CONSEQUENCES IN LIGHT OF THEIR PARTICULAR CIRCUMSTANCES.

Tax Consequences of the Reverse Stock Split

The reverse stock split should constitute a recapitalization for U.S. federal income tax purposes. As a result, a U.S. Holder of Signal common stock generally should not recognize gain or loss upon the reverse stock split, except with respect to cash received in lieu of a fractional share of Signal common stock, as discussed below. A U.S. Holder s aggregate tax basis in the shares of Signal common stock received pursuant to the reverse stock split should equal the aggregate tax basis of the shares of the Signal common stock surrendered (excluding any portion of such basis that is allocated to any fractional share of Signal common stock), and such U.S. Holder s holding period in the shares of Signal common stock received should include the holding period in the shares of Signal common stock surrendered. Treasury Regulations provide detailed rules for allocating the tax basis and

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holding period of the shares of Signal common stock surrendered to the shares of Signal common stock received in a recapitalization pursuant to the reverse stock split. U.S. Holders of shares of Signal common stock acquired on different dates and at different prices should consult their tax advisors regarding the allocation of the tax basis and holding period of such shares.

Cash in Lieu of Fractional Shares

A U.S. Holder of Signal common stock that receives cash in lieu of a fractional share of Signal common stock pursuant to the reverse stock split should recognize capital gain or loss in an amount equal to the difference between the amount of cash received and the U.S. Holder s tax basis in the shares of Signal common stock surrendered that is allocated to such fractional share of Signal common stock. Such capital gain or loss should be long-term capital gain or loss if the U.S. Holder s holding period for Signal common stock surrendered exceeded one year at the effective time of the reverse stock split.

Information Reporting and Backup Withholding

A U.S. Holder of Signal common stock may be subject to information reporting and backup withholding on cash paid in lieu of fractional shares in connection with the reverse stock split. The current backup withholding rate is 28 percent. Backup withholding will not apply, however, to a holder who (i) furnishes a correct taxpayer identification number and certifies the holder is not subject to backup withholding on IRS Form W-9 or a substantially similar form, (ii) provides a certification of foreign status on an appropriate IRS Form W-8 or successor form or (iii) certifies the holder is otherwise exempt from backup withholding. U.S. Holders of Signal common stock should consult their tax advisors regarding their qualification for an exemption from backup withholding and the procedures for obtaining such an exemption. If a U.S. Holder does not provide a correct taxpayer identification number on IRS Form W-9 or other proper certification, the stockholder may be subject to penalties imposed by the IRS. Any amounts withheld under the backup withholding rules may be refunded or allowed as a credit against a U.S. Holder of Signal common stock s federal income tax liability, if any, provided the required information is timely furnished to the IRS. In the event of backup withholding see your tax advisor to determine if you are entitled to any tax credit, tax refund or other tax benefit as a result of such backup withholding.

Required Vote

The affirmative vote of holders of a majority of the outstanding shares of Signal common stock entitled to vote on the record date for the Signal special meeting is required to approve Signal Proposal No. 7. **Each of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9 are conditioned upon each other. Therefore, the Merger cannot be consummated without the approval of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9.**

Recommendation of Board of Directors

SIGNAL S BOARD OF DIRECTORS RECOMMENDS THAT SIGNAL STOCKHOLDERS VOTE FOR SIGNAL PROPOSAL NO. 7 TO APPROVE THE REVERSE STOCK SPLIT.

Signal Proposal No. 8: Approval of the Amendment to the Certificate of Incorporation of Signal to Increase the Number of Authorized Shares of Signal Common Stock.

At the Signal special meeting, Signal stockholders will be asked to approve a proposal to amend Signal s certificate of incorporation to increase the number of authorized shares of Signal common stock from 50,000,000 shares to 100,000,000 shares. A copy of the proposed amendment to Signal s certificate of incorporation is attached as *Annex F*

to this proxy statement/prospectus/information statement.

As of the close of business on the record date, January 9, 2017, Signal had no shares of preferred stock and 742,293 shares of Signal common stock issued and outstanding. As of the close of business on the record date,

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January 9, 2017, there were approximately 315,678 shares of Signal common stock reserved for issuance upon exercise or settlement, as applicable, of outstanding options and restricted stock units and upon conversion of the Note. Based on the number of shares of Miragen preferred stock and common stock outstanding as of such date, if the Merger is completed, Signal would be required to issue approximately 20,156,992 additional shares of Signal common stock to the Miragen stockholders, assuming the closing of Miragen s concurrent financing, as consideration for the Merger, or between 20,156,992 and 1,343,761 shares after giving effect to the reverse stock split. In addition, upon completion of the Merger, Signal would reserve for issuance approximately 4,438,745 additional shares of Signal common stock to cover, among other things, warrants, shares issuable pursuant to the ESPP and stock options, restricted stock, and other stock-based awards assumed from Miragen by Signal, or between 4,438,745 and 295,916 shares after giving effect to the reverse stock split. Signal has determined that the 50,000,000 shares of common stock currently authorized under its certificate of incorporation will be insufficient to satisfy the needs of Signal on a post-Merger basis. It is estimated that following completion of the Merger, Signal will have approximately 24,383,757 shares of common stock available for issuance, or between 24,383,757 to 48,292,291 shares after giving effect to the reverse stock split within a range of one to 15 shares (or any number in between) for every one share of outstanding Signal common stock. Signal s board of directors believes that it is advisable to have additional authorized shares of common stock available for important corporate purposes, such as to provide the ability to react quickly to strategic opportunities and to attract and retain talented employees through the use of equity incentive compensation. Although there are no present plans or commitments for the issuance of any of the additional shares that would be authorized upon approval of this amendment, other than the issuance of shares in connection with the Merger, such additional shares would be available for equity incentive plans, possible future stock splits and dividends, public or private offerings of common stock or securities convertible into common stock, equity-based acquisitions and other corporate purposes that might be proposed. The additional shares of Signal common stock will not be entitled to preemptive rights nor will existing stockholders have any preemptive right to acquire any of those shares when issued.

Required Vote

The affirmative vote of holders of a majority of the outstanding shares of Signal common stock entitled to vote on the record date for the Signal special meeting is required to approve Signal Proposal No. 8. **Each of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9 are conditioned upon each other. Therefore, the Merger cannot be consummated without the approval of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9.**

Recommendation of Board of Directors

SIGNAL S BOARD OF DIRECTORS RECOMMENDS THAT SIGNAL STOCKHOLDERS VOTE FOR SIGNAL PROPOSAL NO. 8 TO APPROVE THE INCREASE IN THE NUMBER OF AUTHORIZED SHARES OF SIGNAL COMMON STOCK.

Proposal No. 9: Approval of the Sale of All of Signal s Intellectual Property Assets Related to its MyPRS Test to Quest Diagnostics Investments LLC

General

At the Signal special meeting, Signal stockholders will be asked to approve an agreement, or the Intellectual Property Purchase Agreement, pursuant to which Signal will sell to Quest Diagnostics Investments LLC the intellectual property assets related to Signal s MyPRS test. These assets are referred to collectively as the MyPRS Assets and they include substantially all of the intellectual property assets through which Signal currently operates its lab business. The sale of the MyPRS Assets will constitute the sale of substantially all of Signal s lab business.

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The Parties

Signal Genetics, Inc.

Signal is a commercial stage, molecular genetic diagnostic company focused on providing innovative diagnostic services that help physicians in the care of their patients suffering from multiple myeloma. Its MyPRS test (included in the MyPRS Assets), a microarray-based gene expression profile assay, is performed in Signal s laboratory located in Little Rock, Arkansas, which is certified under the Clinical Laboratory Improvement Amendments of 1988 and accredited by the College of American Pathologists.

Quest Diagnostics Investments LLC

Quest Diagnostics Investments LLC is a wholly-owned subsidiary of Quest. Quest is the world s leading provider of diagnostic information services. Quest was incorporated in Delaware in 1990; its predecessor companies date back to 1967. Quest conducts business through its headquarters in Madison, New Jersey, and its laboratories, patient service centers, offices and other facilities around the United States and in selected locations outside the United States.

Background and Reasons for the Sale of the MyPRS Assets

Signal is currently marketing and selling its MyPRS test to physicians treating patients suffering from multiple myeloma in academic institutions in all 50 states. Signal has been operating at a net loss since inception, based upon a business plan that anticipated raising additional funds through debt or equity financing to operate beyond the second quarter of 2017. Signal s board of directors considered various factors impacting the financial condition, results and operations for Signal, including Signal s strategic alternatives, the consequences of current market conditions, Signal s current liquidity position, its depressed stock price and continuing net operating losses, the likelihood that the resulting circumstances would not change for the benefit of Signal stockholders in the foreseeable future, and the risks of continuing to operate Signal on a stand-alone basis, including the need to continue building the MyPRS test services menu, infrastructure and management team to support the laboratory services business with insufficient capital resources. Signal came to believe it would be difficult to obtain additional equity or debt financing on acceptable terms, if at all. Therefore, Signal s board of directors began discussing and evaluating its strategic opportunities to maximize stockholder value beginning near the end of 2015. Signal s management provided Signal s board of directors with management s preliminary assessment of a variety of strategic alternatives that Signal could pursue to maximize stockholder value, including engaging in a sale of the company or a merger transaction.

After an extensive process reviewing potential strategic alternatives, as more fully described in *The Merger Background of the Merger*, Signal s board of directors concluded that Signal should pursue a combination with Miragen as such combination would provide the existing Signal stockholders with an opportunity to participate in the potential increase in value of the combined company following the Merger. The wind down of Signal s lab business or divestiture of the MyPRS Assets was also a condition to consummating the Merger in the Merger Agreement.

During the period of July 31, 2016 through October 6, 2016, Mr. Riccitelli and Ms. Seymour met with, either in person or by phone, multiple parties, multiple times for diligence discussions regarding potential acquisition of the MyPRS Assets. All parties were given access to Signal s virtual data room for the purpose of reviewing due diligence materials. During such time, several parties notified Signal management or representatives of Cantor on behalf of Signal that they would not be submitting a proposal to acquire the MyPRS business or any other transaction. The primary reason cited by these parties for not submitting proposals was the additional cash burn required in the near term to continue to offer the MyPRS test commercially.

On August 5, 2016, Mr. Riccitelli and Dr. Bender, Signal s chief medical officer, met with management and medical team personnel from Quest at Quest s Orange County, California facility for an in-depth review of MyPRS.

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On September 30, 2016, Quest submitted an initial LOI to purchase the lab business from Signal, and then submitted a revised LOI on October 10, 2016 to purchase the intellectual property assets related to MyPRS. After a few revisions of the LOI between the parties, on October 19, 2016, Signal s board of directors approved the draft Quest LOI received from Quest on October 18, 2016 and reaffirmed its prior instruction to management to negotiate an asset purchase agreement with Quest, subject to the board s further review of such agreement.

Cantor did not render or express any opinion with respect to, and was not requested to render or express any opinion with respect to, and Cantor s opinion does not address, the sale of the MyPRS Assets, the consideration thereunder or any other aspect thereof.

Between October 27, 2016 and November 23, 2016, there were various teleconferences, in-person meetings, facility tours and email communications among Mr. Riccitelli, Ms. Seymour and Dr. Sur and representatives from Quest s business development, informatics, operations and management teams regarding Quest s due diligence review of Signal s MyPRS test.

During November 2016, Signal was provided a draft intellectual property purchase agreement from Quest that covered the terms of the proposed transaction. Throughout the following weeks, Signal negotiated the terms of the Intellectual Property Purchase Agreement with Quest, and on November 29, 2016, Signal and Quest finalized the terms of the proposed Intellectual Property Purchase Agreement. On November 29, 2016, Signal s board of directors approved by unanimous written consent the final proposed Intellectual Property Purchase Agreement and sale of the MyPRS Assets. Signal s board of directors determined that entering into the Intellectual Property Purchase Agreement and completing the proposed sale of the MyPRS Assets to Quest, subject to stockholder approval and satisfaction of the conditions contained therein, were in the best interests of Signal and its stockholders. Signal s board of directors then approved the Intellectual Property Purchase Agreement and the proposed sale of the MyPRS Assets on the terms set forth in such agreement, and authorized management to execute the Intellectual Property Purchase Agreement on Signal s behalf. On November 29, 2016, Signal and Quest Diagnostics Investments LLC executed the Intellectual Property Purchase Agreement.

Effect of the Sale of the MyPRS Assets

If Signal stockholders approve the sale of the MyPRS Assets to Quest, Signal will seek to complete the sale immediately prior to closing of the Merger with Miragen. The cash proceeds of the proposed sale are $825,000, plus certain expenses, which is expected to be roughly equivalent to Signal s Operating expenses from the time of the LOI to closing of the sale of the MyPRS Assets. Quest has the option to require Signal to operate the lab beyond December 31, 2016 (and through January 14, 2017) for an additional $100,000. The sale is intended to allow Signal to cover its liabilities and other obligations, and is also anticipated to allow Signal to operate until the completion of the Merger and meet the net cash requirement contained in the Merger Agreement.

If Signal stockholders do not approve the sale of the MyPRS Assets to Quest, Signal will be unable to complete the sale pursuant to the Intellectual Property Purchase Agreement with Quest and the lab business will continue to be owned by Signal. Moreover, because the sale, divestiture and/or winding down of Signal s lab business is a closing condition of the Merger Agreement, success of the Merger is also dependent upon stockholder approval of the sale of the MyPRS Assets to Quest. Further, if Signal stockholders do not approve the sale of the MyPRS Assets to Quest and Signal is therefore unable to complete the sale and receive the anticipated cash proceeds, then Signal may incur additional expenses which may not allow Signal to satisfy the closing net cash requirement contained in the Merger Agreement. As a consequence, Miragen will have the right to terminate the Merger Agreement.

The Intellectual Property Purchase Agreement

The following is a description of the material terms of the Intellectual Property Purchase Agreement. The following description does not purport to describe all of the terms and conditions of the Intellectual Property

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Purchase Agreement. The full text of the Intellectual Property Purchase Agreement is attached to this proxy statement/prospectus/information statement as *Annex G* and is incorporated by reference. You are urged to read the Intellectual Property Purchase Agreement in its entirety because it is the legal document that governs the terms and conditions of the proposed sale of the MyPRS Assets.

Included Assets and Retained Liabilities

Pursuant to the Intellectual Property Purchase Agreement, Signal has agreed to sell all of its rights to the MyPRS test, including all of Signal s rights, title and interests to intellectual property assets therein. As part of the sale of MyPRS Assets, Signal will assign all of its rights, interests and obligations under certain agreements, including that certain License Agreement effective as of April 1, 2010, made by and between the Board of Trustees of the University of Arkansas acting for and on behalf of the University of Arkansas for Medical Sciences, a public institution of higher education, and Myeloma Health LLC, a Delaware limited liability company, as amended, collectively referred to herein as the UAMS License Agreement. Signal will also provide to Quest certain information technology, software and firmware related or required for the use of the MyPRS test. As part of the Intellectual Property Purchase Agreement, Signal retains rights to Signal s accounts receivables as of the date the sale of the MyPRS Assets is closed, or the Asset Sale Closing Date. While Quest will not assume any liabilities of Signal, Quest is responsible for all liabilities arising after the Asset Sale Closing Date related to the assigned contracts, other than liabilities arising after the Asset Sale Closing Date due to a breach by Signal of any assigned contracts.

Purchase Price

As consideration for the sale of the MyPRS Assets, Quest will pay to Signal $825,000, plus an additional $100,000 if Quest exercises the option to require Signal to operate the lab until January 14, 2017. Such purchase price will be wire transferred to Signal on or immediately prior to the Asset Sale Closing Date.

Effective Time

The closing of this transaction is anticipated to occur as promptly as practicable after Signal obtains stockholder approval and Signal and Quest satisfy all other conditions to closing.

Representations and Warranties of Signal

The Intellectual Property Purchase Agreement contains representations and warranties customarily included for a seller in similar transactions of this nature relating to, among other things:

Signal s due organization and good standing;

due authorization and corporate authority (including stockholder approval) to enter into the Intellectual Property Purchase Agreement and to consummate the transactions contemplated thereby;

the absence of conflicts or consents required (other than stockholder approval) for Signal to enter into the Intellectual Property Purchase Agreement and related agreements and to consummate the transactions contemplated thereby (including the assignment of the UAMS License Agreement);

the ownership and history of the intellectual property for the MyPRS Assets, including, to Signal s knowledge, the validity and enforceability of the intellectual property for the MyPRS Assets and its absence of infringement;

Signal s exclusive ownership of its rights, title and interest to the MyPRS Assets;

the absence of certain litigation or proceedings with respect to the MyPRS Assets and compliance with applicable laws;

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that Signal s entering into the Intellectual Property Purchase Agreement will not adversely affect Quest s ownership rights with respect to the MyPRS Assets;

the protection and preservation of the chain of title for the MyPRS Assets and the confidential information and trade secrets related thereto;

the lack of contracts providing for the license, sale or encumbrance of the MyPRS Assets and the validity and enforceability of the agreements assigned to Quest (including the UAMS License Agreement);

taxes with respect to the MyPRS Assets;

the value of the MyPRS Assets and the consideration being paid by Quest;

the solvency of Signal (taking into consideration the payment of the purchase price); and

that Signal is not obligated to pay fees to any brokers other than Cantor.

The assertions embodied in the representations and warranties made by Signal are qualified by Signal s knowledge in certain instances and information set forth in a confidential schedule delivered in connection with the Intellectual Property Purchase Agreement. While Signal does not believe that the schedule contains information that securities laws require it to publicly disclose, other than information that is being disclosed in this proxy statement/prospectus/information statement, the schedule may contain information that modifies, qualifies and creates exceptions to the representations and warranties set forth in the Intellectual Property Purchase Agreement. Accordingly, you should not rely on any of these representations and warranties as characterizations of the actual state of facts, since they may be modified in important respects by the underlying schedule.

Representations and Warranties of Quest

The Intellectual Property Purchase Agreement contains representations and warranties customarily included for a buyer in similar transactions of this nature relating to, among other things:

Quest s due organization and good standing;

due authorization and limited liability company authority to enter into the Intellectual Property Purchase Agreement and to consummate the transactions contemplated thereby;

the consents required to enter into the Intellectual Property Purchase Agreement and to consummate the transactions contemplated thereby;

the enforceability of the Intellectual Property Purchase Agreement against Quest; and

that Quest entering into the Intellectual Property Purchase Agreement and consummating the transactions contemplated thereby will not result in a conflict with its charter documents, certain legal requirements or certain agreements.

Non-Solicitation

From November 29, 2016 until the Asset Sale Closing Date, Signal is prohibited from directly or indirectly soliciting, initiating, encouraging, accepting or entertaining any inquiries, offers or proposals from any other person or entity relating to any asset sale or similar transaction involving the MyPRS Assets (with the exception of operating the MyPRS test in the ordinary course of its business).

Assignment of Agreements

As part of the sale of the MyPRS Assets, Signal will assign to Quest various agreements, including the UAMS License Agreement. Quest agrees to be bound by the terms, obligations and conditions as a licensee under the UAMS License Agreement pursuant to an assignment and assumption agreement.

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Closing Conditions

Under the terms of the Intellectual Property Purchase Agreement, there are several conditions to closing. Among such conditions, neither Signal nor Quest is obligated to close the sale of the MyPRS Assets if there is a court order or injunction prohibiting the sale of the MyPRS Assets, or if Signal has not obtained stockholder approval for the sale of the MyPRS Assets or the Merger Agreement.

Signal s and Quest s obligation to close are contingent upon additional customary closing conditions including, without limitation, the following: (i) accuracy of certain representations and warranties as set forth in the Intellectual Property Purchase Agreement; (ii) performance of other agreements, covenants and conditions under the Intellectual Property Purchase Agreement; (iii) execution of certain documents by the parties and delivery of certain closing certificates specified in the Intellectual Property Purchase Agreement.

Termination

The Intellectual Property Purchase Agreement may be terminated due to a number of reasons, including: (i) by mutual written consent of Quest and Signal; (ii) if there has been a material breach, inaccuracy or failure to perform any of the representations, warranties, covenants or agreements of a party as set forth in the Intellectual Property Purchase Agreement; (iii) the Asset Sale Closing Date has not occurred on or before April 30, 2017 (unless agreed to otherwise); (iv) the Merger Agreement has been terminated; (v) any law makes such sale illegal or otherwise prohibited; (vi) a governmental authority issues an order preventing or enjoining the consummation of the transaction; or (vii) a proceeding or investigation seeks material damages in connection with the Merger or the sale of the MyPRS Assets.

Expenses

Signal and Quest are each responsible for their respective costs and expenses that Signal or Quest incur in connection with the proposed sale of the MyPRS Assets.

Indemnification

Certain of Signal s representations and warranties survive the closing for a period of 12 months and others remain in force and effect for 18 months. Under the Intellectual Property Purchase Agreement, Signal is required to indemnify Quest for any breaches of Signal s representations, warranties, covenants and agreements during the applicable survival period and with respect to any retained liabilities and therefore Signal will have continuing potential liability to Quest following the closing. Quest agrees to indemnify Signal under the Intellectual Property Purchase Agreement for any breaches of Quest s representations, warranties or covenants and any assumed liabilities.

The Intellectual Property Purchase Agreement limits Signal s aggregate liability for indemnification with respect to the breach of certain representations and warranties to $825,000 and $206,250 of this amount for the breach of other representations and warranties and such indemnification is subject to a nuisance provision such that Signal s indemnification obligations are not triggered unless the aggregate amount of a claim, demand or loss exceeds $41,250, after which Signal will be obligated for the full amount of losses.

Accounting Treatment

Signal will record the sale of the MyPRS Assets in accordance with U.S. GAAP.

Government Approvals

Signal is not aware of any federal or state regulatory requirements that must be complied with or approvals that must be obtained to complete the sale of the MyPRS Assets, other than the filing of this proxy statement/

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prospectus/information statement with the SEC. If any additional approvals or filings are required, Signal will use commercially reasonable efforts to obtain those approvals and make any required filings before completing the transactions.

No Appraisal Rights

Signal stockholders do not have appraisal rights under the DGCL in connection with the sale of the MyPRS Assets.

Required Vote

The affirmative vote of holders of a majority of the outstanding shares of Signal common stock entitled to vote on the record date for the Signal special meeting is required to approve Signal Proposal No. 9. **Each of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9 are conditioned upon each other. Therefore, the Merger cannot be consummated without the approval of Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8 and 9.**

Recommendation of Board of Directors

SIGNAL S BOARD OF DIRECTORS RECOMMENDS THAT THE SIGNAL STOCKHOLDERS VOTE FOR SIGNAL PROPOSAL NO. 9 TO APPROVE THE SALE OF ALL OF SIGNAL S INTELLECTUAL PROPERTY ASSETS RELATED TO ITS MYPRS TEST TO QUEST DIAGNOSTICS INVESTMENTS LLC.

Signal Proposal No. 10: Approval of the Amendment to the Certificate of Incorporation of Signal to Eliminate the Ability of Signal Stockholders to Act by Written Consent.

At the Signal special meeting, Signal stockholders will be asked to approve a proposal to amend Signal s certificate of incorporation to eliminate the ability of stockholders to act by written consent. A copy of the proposed amendment to Signal s certificate of incorporation is attached as *Annex H* to this proxy statement/prospectus/information statement. The Merger Agreement requires that Signal seek stockholder approval to eliminate the ability of stockholders to act by written consent, although obtaining such stockholder approval is not a condition to closing the Merger.

Section 228 of the DGCL provides that, unless otherwise provided in a company s certificate of incorporation, any action that may be taken at any annual or special meeting of stockholders may be taken without a meeting, without prior notice to all stockholders and without holding a vote, if a consent in writing is signed by stockholders representing the minimum number of votes necessary to approve the action at a meeting at which all shares entitled to vote thereon were present and voted. Signal stockholders currently have the ability to act by written consent because Signal s certificate of incorporation does not contain a provision eliminating the right of stockholders to act by written consent. If Signal stockholders adopt this proposed amendment to Signal s certificate of incorporation, the power of its stockholders to act without a meeting by written consent will be eliminated. Signal s board of directors has determined that removing the ability of the stockholders to act by written consent without a meeting is in the best interests of Signal and its stockholders.

Signal s board of directors values the exchange of thoughts and views with all of its stockholders, is committed to being highly responsive to stockholder interests and concerns and has carefully considered the advantages and disadvantages of eliminating the ability of stockholders to act by written consent and has determined that it is appropriate to adopt this proposed amendment to Signal s certificate of incorporation. In particular, Signal s board of directors has noted that the written consent process, by its nature, is not conducive to an orderly and transparent discussion on the merits of a proposed action, as would occur if the action were raised at a meeting of stockholders. Even if Signal eliminates the ability of its stockholders to act by written consent, proposals for stockholder action,

such as proposed amendments to Signal s bylaws or the removal of one or more of Signals

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directors, could still take place at the Signal annual meeting of stockholders. The process for proposing and discussing matters at an annual meeting is well-established and specifically designed to provide stockholders and Signal s board of directors adequate time to review, evaluate, discuss and consider a proposed action. The written consent process does not foster these characteristics and can be subject to abuse. For example, a dissident stockholder holding a small number of Signal s outstanding common stock would be able to launch an unsolicited consent solicitation to change the make-up of Signal s board of directors. Because Signal s certificate of incorporation permits stockholders to take action by written consent, this dissident stockholder would be able to commence this process without ever approaching Signal or Signal s board of directors to express any concerns or ideas. The consent solicitation could result in an expensive and time-consuming distraction to Signal s operational efforts, even if only a small number of shares ultimately support the dissident s proposals.

The proposed amendment also provides various additional benefits. For example, the amendment could reduce the time and effort Signal s board of directors and management would need to devote to stockholder proposals, which time and effort could distract its directors and management from other important company business. In addition, the amendment would make it difficult for a person who acquires a majority of the outstanding common stock of Signal to approve a merger or sale of Signal or take other action normally requiring a vote of stockholders without providing notice to all stockholders and convening a meeting to vote on the proposed action. Signal s board of directors believes that the benefits of discouraging hostile bidders and dissident stockholders seeking to further their own special interests from conducting potentially expensive and disruptive consent solicitations outweigh the inconvenience of needing to act at the Signal annual meeting of stockholders.

In light of the foregoing, as well as the covenant in the Merger Agreement requiring Signal to seek stockholder approval, Signal s board of directors believes that amending its certificate of incorporation to eliminate stockholder action by written consent is a prudent corporate governance measure. The proposed text relating to the amendment to Signal s certificate of incorporation to eliminate the ability of stockholders to act by written consent as it is proposed to be amended is attached as *Annex H* to this proxy statement/prospectus/information statement.

If Signal stockholders approve this proposal, Signal anticipates that its board of directors will approve a corresponding amendment to Signal s bylaws.

Potential Anti-Takeover Effect and Other Provisions

The proposal to eliminate the ability of Signal stockholders to act by written consent could have a potential anti-takeover effect. The effect of the proposal might render more difficult or discourage a merger, tender offer, proxy contest or change in control and the removal of management, which Signal stockholders might otherwise deem favorable. The proposal, if adopted, may be disadvantageous to Signal stockholders to the extent that it has the effect of delaying or discouraging a future takeover attempt that is not approved by Signal s board of directors but which a majority of Signal stockholders may deem to be in their best interests. The amendment to Signal s certificate of incorporation is not being proposed in response to any attempt to acquire control of Signal, to obtain representation on Signal stockholders, or to take significant corporate action and Signal is not aware of any such plans, other than the Merger. Signal s board of directors does not currently have any plans to implement additional measures that may have an anti-takeover effect other than those actions described in this proxy statement/prospectus/information statement.

Required Vote

The affirmative vote of holders of a majority of the outstanding shares of Signal common stock entitled to vote on the record date for the Signal special meeting is required to approve Signal Proposal No. 10.

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Recommendation of Board of Directors

SIGNAL S BOARD OF DIRECTORS RECOMMENDS THAT SIGNAL STOCKHOLDERS VOTE FOR SIGNAL PROPOSAL NO. 10 TO APPROVE THE ELIMINATION OF THE ABILITY OF SIGNAL STOCKHOLDERS TO ACT BY WRITTEN CONSENT.

Signal Proposal No. 11: Approval of Possible Adjournment of the Signal Special Meeting

If Signal fails to receive a sufficient number of votes to approve Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10, Signal may propose to adjourn the Signal special meeting, for a period of not more than 30 days, for the purpose of soliciting additional proxies to approve Signal Proposal Nos. 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10. Signal currently does not intend to propose adjournment at the Signal special meeting if there are sufficient votes to approve Signal Proposal 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10.

Required Vote

The affirmative vote of the holders of a majority of the shares of Signal common stock having voting power present in person or represented by proxy at the Signal special meeting is required to approve Signal Proposal No. 11.

Recommendation of Board of Directors

SIGNAL S BOARD OF DIRECTORS RECOMMENDS THAT THE SIGNAL STOCKHOLDERS VOTE FOR SIGNAL PROPOSAL NO. 10 TO ADJOURN THE SIGNAL SPECIAL MEETING, IF NECESSARY, TO SOLICIT ADDITIONAL PROXIES IF THERE ARE NOT SUFFICIENT VOTES IN FAVOR OF SIGNAL PROPOSAL NOS. 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10.

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SIGNAL BUSINESS

Overview

Signal is a commercial stage, molecular genetic diagnostic company focused on providing innovative diagnostic services that help physicians make better-informed decisions concerning the care of their patients suffering from cancer. Its mission is to develop, validate and deliver innovative diagnostic services that enable better patient-care decisions. The patient-care decisions include the field of personalized medicine, wherein diagnostic tests guide treatment decisions with genetically-targeted therapies as well as traditional chemotherapy regimens. Signal holds an exclusive license in its licensed field to the intellectual property stemming from the renowned research on multiple myeloma, or MM, performed at the University of Arkansas for Medical Sciences, or UAMS.

Signal is currently marketing and selling its MyPRS test to physicians treating patients suffering from MM in academic institutions in all 50 states. Its MyPRS test is performed in Signal s approximately 2,800 square foot laboratory located in Little Rock, Arkansas, which is certified under CLIA and accredited by CAP to perform high complexity testing. Signal s MyPRS test is a microarray-based Gene Expression Profiling, or GEP, assay that tests for the presence of specific groups of genes that can predict low or high level risk of early relapse in patients suffering from MM. The information provided by Signal s MyPRS test aids physicians in selecting the optimal treatment regimen for each patient s unique MM condition. To Signal s knowledge, it is the only company marketing a GEP test for assessing the status of MM in the United States. The MyPRS test is protected by a substantial patent portfolio of issued and pending patents.

Signal has been operating at a net loss since inception, based upon a business plan that anticipated raising additional funds through debt or equity financing to operate beyond the second quarter of 2017. Due to current market conditions, Signal s current liquidity position and its depressed stock price, Signal came to believe it would be difficult to obtain additional equity or debt financing on acceptable terms, if at all. Therefore, Signal s board of directors began discussing and evaluating its strategic opportunities to maximize stockholder value beginning near the end of 2015, including engaging in a sale of the company or a merger transaction.

In April 2016, Signal engaged Cantor as its exclusive financial advisor in connection with exploring and assessing strategic opportunities in connection with a possible sale or merger, as well as its exclusive financial advisor and placement agent in connection with a potential capital raise for equity or debt capital. Cantor was selected by Signal due to its substantial experience with the healthcare industry and transactions similar to this transaction. Signal conducted a process of identifying and evaluating potential strategic combinations or the sale of substantially all of its assets. On October 31, 2016, Signal, Merger Sub and Miragen entered into the Merger Agreement, pursuant to which, among other things, subject to the satisfaction or waiver of the conditions set forth in the Merger Agreement, Merger Sub will merge with and into Miragen, with Miragen becoming a wholly-owned subsidiary of Signal and the surviving corporation of the Merger. If the Merger is completed, the business of Signal will become the business of Miragen as described in this proxy statement/prospectus/information statement under the caption *Miragen Business*.

On October 31, 2016, Signal also announced that it had entered into a non-binding letter of intent with a large global diagnostic laboratory for the sale of intellectual property assets related to Signal s MyPRS test. Subsequently on November 29, 2016, Signal and Quest Diagnostics Investments LLC entered into the Intellectual Property Purchase Agreement. Pursuant to the Intellectual Property Purchase Agreement, upon closing of the sale of the MyPRS asset transaction, Signal will receive $825,000 in cash from Quest. These net proceeds are currently expected to be approximately equal to the anticipated costs of operating the MyPRS business from the date of signing of the letter intent through the projected closing date of the Merger with Miragen (resulting, from a cash perspective, in an outcome similar to an immediate cessation of the MyPRS business). Completion of the MyPRS asset sale is subject to

satisfaction of the conditions contained in the definitive asset purchase agreement and approval of the sale by Signal stockholders, as further described in this proxy statement/prospectus/information statement.

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If the Merger and the sale of intellectual property assets related to Signal s MyPRS test are not completed, Signal will reconsider its strategic alternatives and would likely dissolve and liquidate its assets. In such event, Signal would be required to pay all of its debts and contractual obligations, and to set aside certain reserves for potential future claims, and there can be no assurances as to the amount or timing of available cash remaining to distribute to stockholders after paying the Signal obligations and setting aside funds for reserves.

Signal s Intellectual Property

Signal uses its trademark of Signal Genetics, Inc.™ and registered trademark MyPRS® in this proxy statement/prospectus/information statement.

Signal currently licenses, or owns outright, 14 issued patents (12 issued U.S. patents, one issued European patent validated in 9 countries: Switzerland, Germany, Denmark, Spain, France, United Kingdom, Italy, Netherlands, and Sweden, and one issued Japanese patent with various expiration dates ranging from 2022 to 2030) and 11 pending patent applications, many of which protect and defend its exclusive ability to market the MyPRS test as well as additional proprietary tests and treatments. Signal also has six registered U.S. trademarks to further differentiate its products and services in the marketplace.

There are two issued U.S. patents related to the MyPRS test, which form the basis of Signal s right to exclude others from practicing the MyPRS test. The patents claim methods of gene expression-based classification for MM using RNA from plasma cells, methods of identifying groups of genes that can distinguish normal and MM plasma cells by isolating RNA from CD138 positive plasma cells and identifying differentially expressed genes, methods of diagnosing MM by examining mRNA levels or chromosomal translocations of particular genes from plasma cells, methods of determining the prognosis of a human multiple myeloma patient by measuring gene expression levels of multiple genes from plasma cells, and methods of determining the prognosis of a MM patient by determining the copy number of the CKS1B gene in plasma cells. CKS1B is one of the genes in the 70 gene signature.

In addition to the issued U.S. patents, Signal has one issued Japanese patent and several pending patent applications in the United States and abroad directed to other aspects of the MyPRS test. For example, the Japanese patent provides methods for examining the susceptibility of a subject for transformation from a low-risk to a high-risk MM by measuring gene expression levels of multiple genes expressed from plasma cells isolated from the subject. A Canadian application and an issued European counterpart patent of one of the five issued U.S. patents (U.S. Patent No. 8,843,320) describe the full 70 gene signature used in the MyPRS test. Another pending U.S. application provides methods of prognosing subjects with MGUS using the 70 gene signature.

Competition

The primary competition for the MyPRS test stems from the use of older diagnostic technologies to assess patient prognosis and to define high risk and low risk MM patients. These older technologies include various serum markers, karyotype analysis and FISH probes. Several independent groups have assessed the use of GEP versus various conventional methodologies and these studies have been published in peer-reviewed journals.

Another source of competition for the MyPRS test stems from other scientific teams attempting to develop GEP signatures utilizing other genes or a subset of the genes utilized in the MyPRS test. Two signatures of note include the French IFM-15 gene signature and the Netherlands EMC-92 gene signature which have been studied by independent groups and compared to the UAMS GEP test, MyPRS. Signal is not currently aware of any company attempting to bring GEP based tests into the U.S. market.

Signal s actual and potential competitors in the United States and abroad may include biotechnology, genomic and diagnostic companies such as Novartis, Cancer Genetics, Inc. and NeoGenomics, Inc., Bio-Reference Laboratories (a division of OPKO Health, Inc.)., Integrated Genetics (a LabCorp Specialty Testing Group) and Foundation Medicine, Inc., large clinical laboratories, universities and other research institutions.

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University of Arkansas License Agreement

In April 2010, Signal entered into a licensing agreement with UAMS for the exclusive use, in Signal s licensed field, of intellectual property developed at the Myeloma Institute of UAMS consisting of patents used in the GEP assay, MyPRS and its related technology through April 2020. The agreement is effective through the earlier of the expiration of the related patents or termination of the agreement pursuant to its terms. Signal may terminate the agreement for any reason upon 90 days written notice. UAMS may terminate the agreement with 90 days written notice upon a material breach of the agreement by Signal or if Signal challenges the validity of any licensed patent in a court of competent jurisdiction. Under the terms of the license agreement, Signal is required to pay $30,000 in annual minimum royalties on sales to customers other than UAMS unless sales, as defined in the agreement, exceed certain thresholds in which case the additional royalties would range from 2% 4%. Total royalty expense during each of the years ended December 31, 2015 and 2014 was $30,000.

Revenue sourced from or through UAMS accounted for 54% and 84% of Signal s net revenue for the years ended December 31, 2015 and 2014, respectively, and accounted for 22% and 64% of Signal s net revenue during the nine months ended September 30, 2016 and 2015, respectively. The decrease is due to the decrease in research funds available at UAMS for such programs. Signal expects continued declining revenue from the UAMS research programs.

Government Regulation

Clinical Laboratory Improvement Amendments

Signal is subject to CLIA, which is administered by the Center for Medicare and Medicaid Services, or CMS, and extends federal oversight to virtually all clinical laboratories by requiring certification by the federal government or by a federally-approved accreditation agency.

New York State Laboratory Licensing

New York state laws and regulations also establish standards for the day-to-day operations of clinical laboratories, including physical facility requirements and equipment and quality control. New York standards include proficiency testing requirements, even for a laboratory not located within the state. In addition, the New York Department of Health separately approves certain Laboratory Developed Test, or LDT, offered in New York State. In June 2014, following Signal s initial public offering, it obtained the requisite approvals for its LDT in New York. Such license expires in June 2017.

Other States Laboratory Testing

In addition to New York, certain other states, including California, Florida, Maryland, Pennsylvania, and Rhode Island require that Signal hold licenses to test specimens from patients residing in those states even though Signal s laboratory is physically located in Arkansas. Signal has obtained licenses in these states and believes it is in material compliance with its applicable licensing laws.

Other Laboratory Regulations

Signal s clinical operations are also subject to regulation under state laws that may be more stringent than CLIA. State clinical laboratory laws generally require that laboratories and/or laboratory personnel meet certain qualifications. State clinical laboratory laws also generally require laboratories to specify certain quality controls and maintain

certain records.

HIPAA Compliance and Privacy Protection and the HITECH Act

HIPAA and its implementing regulations established comprehensive federal protection for the privacy and security of health information. The HIPAA standards apply to three types of organizations, or Covered

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Entities : health plans, health care clearing houses, and health care providers who conduct certain health care transactions electronically, or Standard Transactions. Covered Entities must have in place administrative, physical and technical safeguards to protect against the misuse of individually identifiable health information, or PHI. Additionally, some state laws impose privacy and security protections more stringent than HIPAA s and some states impose privacy and security obligations specifically applicable to clinical laboratories. Additionally, many states have implemented data breach laws requiring additional security measures for certain types of PHI and also public notification of the theft, breach or other loss of personal information. Signal is a Covered Entity subject to the HIPAA regulations because its testing services are reimbursable by insurance payors and it conducts Standard Transactions. Signal has an active program designed to address HIPAA regulatory compliance.

Additionally, the HITECH Act and the regulations promulgated thereunder by the HHS require HIPAA covered entities, including clinical laboratories, to provide notification to affected individuals and to the Secretary of HHS, following discovery of a breach of unsecured PHI. In some cases, the HITECH Act requires covered entities to provide notification to the media of breaches. In the case of a breach of unsecured PHI at or by a business associate of a covered entity, the HITECH Act requires the business associate to notify the covered entity of the breach. The HITECH Act requires the Secretary of HHS to post on the HHS website a list of covered entities that experience breaches of unsecured PHI involving more than 500 individuals. The HITECH Act made other changes relating to the HIPAA privacy and security rules, including, among others, establishing that, effective February 17, 2010, the HIPAA security and certain privacy regulations apply directly to business associates and, consequently, that a business associate s violation of the HIPAA regulations may result in government enforcement action directly against the business associate or the covered entity with whom the business associate contracts depending upon the nature of that business relationship. Signal contracts with business associates to provide certain services regulated by the HIPAA regulations and therefore must comply with the HIPAA regulations governing those business relationships.

In summary, Signal is required to comply with laws governing the transmission, security and privacy of health information that require significant compliance costs, and any failure to comply with these laws could result in material criminal and civil penalties.

Research and Development Program

Signal s research and development expenses were $1.0 million and $347,000 for the years ended December 31, 2015 and 2014, respectively, representing 39% and 8% of its net revenue for the years ended December 31, 2015 and 2014, respectively. Signal s research and development expenses were $226,000 and $253,000 for the nine months ended September 30, 2016 and 2015, respectively, representing 34% and 29% of its net revenue for the nine months ended September 30, 2016 and 2015, respectively.

Employees

As of December 31, 2016, Signal had 17 employees, all of whom are full-time employees. None of its employees is represented by a labor union, and Signal considers its relationship with its employees to be good.

Properties

Signal currently leases 5,560 square feet of office space in Carlsbad, California, for its corporate headquarters. This lease expires in October 2017. Signal also leases 2,800 square feet of space in Little Rock, Arkansas for use as a clinical reference laboratory. This lease terminates in January 2017.

Legal Proceedings

Signal is not currently a party to any legal proceedings.

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MIRAGEN BUSINESS

Overview

Miragen is 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. Miragen believes its 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. Miragen uses its expertise in systems biology and oligonucleotide chemistry to discover and develop a pipeline of product candidates. Miragen s two lead product candidates, MRG-106 and MRG-201, are currently in Phase 1 clinical trials. Miragen s 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. Miragen s 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 Miragen s clinical programs, it is developing a pipeline of pre-clinical product candidates. The goal of Miragen s 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) and safety of the product candidate in pre-clinical studies.

In February 2016, Miragen administered MRG-106 to the first patient in a multi-site, open-label, dose-ranging Phase 1 clinical trial that seeks to enroll up to 50 patients with a confirmed diagnosis of mycosis fungoides, or MF, which is a subtype of cutaneous T-cell lymphoma, or CTCL, in which malignant T-cells move to the skin and form patches (palpable flat lesions) or plaques and tumors. MRG-106 has been generally safe and well tolerated in the six patients who received the product candidate in Part A, with no significant injection site reactions or dose limiting toxicities. In addition, molecular analyses of patient tissue samples demonstrated changes in gene expression in the tumors consistent with what Miragen believes is the expected mechanism of action of MRG-106 in CTCL lesions. Miragen believes that these data demonstrate the potential of MRG-106 to regulate gene pathways to provide clinical benefit in MF patients. MRG-106 has been generally safe and well tolerated in the eight patients who have received the product candidate in Part B, with no significant injection site reactions.

In November 2015, Miragen initiated a single-center Phase 1, double-blind, placebo-controlled, single and multiple dose-escalation clinical trial of MRG-201 enrolling up to 70 healthy volunteers. Forty-seven volunteers have enrolled in the trial, 40 of whom have received MRG-201. MRG-201 has been generally safe and well-tolerated in all volunteers, with no significant injection site reactions. Biomarker analysis demonstrated on-target molecular activity for MRG-201 in human skin, with an apparent dose-dependent effect after a single dose. Preliminary histological analysis indicates that incisions treated with MRG-201 generally showed a decrease in formation of fibrous tissue, or fibroplasia, with no apparent detrimental effect on wound healing. Miragen believes these data suggest that MRG-201 may be able to reduce pathological fibrosis and scar formation in human skin.

In addition to MRG-106 and MRG-201, Miragen has a pipeline of wholly-owned, pre-clinical product candidates that target individual microRNAs thought to be at abnormally high or low levels in particular diseases. Miragen believes its experience in microRNA biology and chemistry, drug discovery, bioinformatics, and translational medicine allows it to identify and develop RNA-targeted drugs that are designed to regulate gene pathways to return diseased cells to a healthy state. Miragen believes that its drug discovery and development strategy will enable it to progress its product candidates from pre-clinical discovery to demonstration of mechanism of action in humans quickly and efficiently.

The elements of this strategy include identification of biomarkers that may predict clinical benefit and monitoring outcomes in early-stage clinical trials to help guide later clinical development.

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The following table illustrates Miragen s most advanced programs:

Product Candidate	Target	Disease Area	Development Status
Clinical			
MRG-106	miR-155	Blood Cancers	Phase 1 clinical trial
MRG-201	miR-29	Pathological Fibrosis	Phase 1 clinical trial
Pre-Clinical			
MRG-107	miR-155	Neuro-Inflammation	IND Enabling
MRG-110	miR-92	Revascularization	IND Enabling
Unnamed	TBA	Cardiovascular	Lead Optimization

Miragen s Strategy

Miragen seeks to use its expertise and understanding of microRNA biology, oligonucleotide chemistry and product development to create novel products that have the potential to transform the treatment of patients with serious diseases. The key components of Miragen s strategy are as follows:

Continue to develop MRG-106 in blood cancers. Miragen s ongoing Phase 1 clinical trial of MRG-106 for the treatment of patients with MF is designed to deliver the necessary data and mechanistic proof-of-concept to support further development of miR-155 inhibitor, MRG-106, in multiple cancer indications in which elevated levels of miR-155 has been observed. Miragen plans to expand its clinical program to explore the broader utility of MRG-106 in patients with other blood cancers, such as diffuse large B cell lymphoma and virally induced lymphomas. Miragen also intends to initiate a Phase 2 clinical trial of MRG-106 in CTCL using a dose, schedule and route of administration selected based on results obtained in the Phase 1 clinical trial.

Continue to develop MRG-201 in pathological fibrosis. Miragen s ongoing Phase 1 clinical trial of MRG-201 in healthy volunteers, in addition to being a safety and tolerability trial, is designed to serve as a human mechanistic proof-of-concept assessment that helps reduce the risk associated with further development of the product candidate for other forms of pathological fibrosis such as pulmonary, retinal, hepatic and renal fibrosis. This clinical trial may serve as a prelude to a Phase 2 clinical trial in skin manifestations of pathological fibrosis. Miragen may pursue additional development of MRG-201 independently or through a strategic alliance.

Utilize rare disease development pathways at the FDA and comparable foreign regulatory agencies to accelerate progression to late stage development and early approval. For wholly-owned programs, Miragen intends to focus on rare and genetically stratified diseases where RNA modulation may produce clinical benefit so that Miragen can take advantage of regulatory programs intended to expedite drug development. Miragen plans to apply for the regulatory programs for orphan drug designation, fast track, breakthrough therapy designation, and/or priority review when available to potentially reduce clinical trial expense and increase speed to commercialization.

Collaborate with other biotechnology and pharmaceutical companies to develop additional product candidates. Miragen intends to seek out collaborations for additional microRNA targets and development of compounds in Miragen s pipeline that require larger clinical trials or extensive commercial infrastructure. For example, Miragen has a multi-target strategic collaboration with Servier to develop product candidates for the treatment of cardiovascular diseases.

Use its in-house research and translational expertise to further develop its product candidate pipeline. Miragen s in-house research team investigates novel microRNA targets identified through internal efforts and academic collaborations. It then seeks to establish evidence that the microRNA is implicated in certain diseases. Miragen believes that this internal research and expertise could provide a foundation to develop product candidates for the treatment of a variety of diseases in which microRNA is implicated.

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Selectively build focused commercial capabilities and establish commercial collaborations to maximize the value of Miragen s pipeline. To date, Miragen has retained all U.S. and Japanese rights to its product candidates in the strategic collaboration with Servier and global rights in all other programs. While Miragen has not yet defined its sales, marketing or product distribution strategy for MRG-106, MRG-201 or any of its other product candidates, its commercial strategy may include the use of strategic alliances, distributors, a contract sales force, or the establishment of its own commercial and specialty sales force to maximize the value of its pipeline.

Miragen s Product Candidates

MRG-106

MRG-106, is an inhibitor of miR-155. Miragen is conducting a Phase 1 clinical trial of MRG-106 in patients with MF. Scientific literature identifies miR-155 as a cancer-causing microRNA, or oncomiR with a central role in the development of multiple blood cancers. miR-155 controls a number of validated disease targets, including Bruton s Tyrosine Kinase and nuclear factor kappa-light-chain-enhancer of activated B cells. In certain B-cell lymphomas, improvement of clinical outcomes has been associated with normalization of miR-155 levels, and poor prognosis, resistance to treatment and recurrence of the disease are associated with elevated levels of miR-155. In addition to playing a role in B-cell malignancies, miR-155 is elevated in malignant white blood cells, called T-cells, found in skin lesions of patients with MF. Miragen screened a library of locked nucleic acid modified oligonucleotides, and identified MRG-106 as having what Miragen believed was the best potential efficacy and drug-like properties including improved pharmacodynamics in human T- and B-cell lymphoma cell lines.

Mycosis Fungoides

MF is the most common form of a type of blood cancer called CTCL. CTCL occurs when T-cells become cancerous. These types of cancers cause different types of skin lesions. Although the skin is involved, the skin cells themselves are not cancerous. According to the National Institutes of Health, or NIH, MF usually occurs in adults over age 50, although the disease may occur in children.

Miragen believes the total population of patients with cutaneous lymphoma in the United States and Canada is approximately 30,000. In a 2012 publication, the Lymphoma Research Foundation estimated the prevalence of MF to be 16,000-20,000 cases in the United States. According to the Leukemia and Lymphoma Society in a 2014 publication, approximately 70% to 80% of patients are diagnosed with early stage MF that impacts only the skin. In these patients, the disease typically has a slow progression, but is accompanied by serious quality of life detriments such as severe itchiness, pain and disfiguration. The five-year survival rate for newly diagnosed patients with CTCL is approximately 90%. In later stage MF and in some early stage patients whose disease progresses, the cancer may involve the lymph nodes, blood and internal organs. The five-year survival rate in later stage patients with CTCL (stages IIB, III, IV) is approximately 20-60% depending on stage.

There are currently no curative therapies for CTCL, and concurrent and consecutive treatments, many with significant adverse events, tend to be given until loss of response. There is a need for new and improved therapies in CTCL to treat the disease and eliminate symptoms such as itchiness and painful skin lesions and to prolong survival in patients with aggressive disease. Most drugs for CTCL have response rates between 30 and 40%, and response durations tend to be less than a year.

There is no standard of care for treatment of MF. Treatment is dependent on stage of disease and responsiveness to previous therapy and is divided into skin-directed therapy and whole body treatments. For certain patients with advanced disease, allogeneic stem cell transplantation may offer prolonged survival, but the five-year survival is only

around 50%.

In addition to MF, the elevation of miR-155 has been implicated in several other blood cancers and certain solid tumors. Miragen believes there is a potential opportunity to develop a companion diagnostic that could detect and

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quantify levels of miR-155 in malignant cells. Miragen believes this approach may then allow for the selection of patients with elevated miR-155 levels who may be more likely to benefit from MRG-106 treatment and allow the drug to be used selectively in multiple cancers. There are several types of cancer in which high levels of miR-155 have been discovered, including subsets of diffuse large B-cell lymphoma, acute myeloid leukemia, certain virally induced lymphomas such as HTLV-1 associated lymphoma and Burkitt s lymphoma, Down Syndrome-associated acute lymphocytic leukemia, and other types of cancer. Miragen plans to evaluate additional types of lymphoma and leukemia in Phase 1 clinical trials and intends to explore other potential applications for MRG-106 through additional clinical studies in other tumor types.

MRG-106 Phase 1 Clinical Trial

Trial Design

Miragen is conducting a multi-site, open-label, dose-ranging Phase 1 clinical trial of MRG-106 for the treatment of MF at 11 U.S.-based clinical sites. This clinical trial consists of two parts and is expected to enroll up to 50 patients with MF. Patients may be allowed to be on other medications or background therapies so long as they have had no change in treatment regimen for CTCL, including drug and dose, for more than four weeks prior to enrollment and, in the opinion of the investigator, the patient is currently clinically stable and is likely to remain clinically stable for a minimum of three months after screening.

The primary objectives of this clinical trial are safety and tolerability. Secondary objectives include pharmacokinetic assessments, including measurement of absorption and clearance of MRG-106 from the blood. Additionally, there are several exploratory measures to assess any changes in lesion severity before and after treatment as well as pharmacodynamic and histology assessments. The clinical trial utilizes two validated measures of lesion severity: (i) CAILS, which is a composite measure that assesses the severity of one or more lesions on a patient and (ii) modified Severity Weighted Assessment Tool, or mSWAT, which is an assessment tool that is used to analyze the disease severity over a patient s entire body.

Part A of the clinical trial tested the effect of direct injections of 75 mg of MRG-106 intratumorally. Part A of the clinical trial enrolled six patients, five of whom completed dosing. One patient was withdrawn from the trial due to disease progression. In four patients, saline placebo was injected into a separate skin lesion at the same time. After eight to 14 days of treatment, in five patients, injections sites were biopsied and analyzed for drug concentration, molecular evidence of drug activity on target gene expression, and histological evidence of alterations in malignant cell numbers and other immune cell populations. Additionally, as an exploratory endpoint, CAILS scoring was used to assess clinical response.

Part B of the clinical trial is enrolling patients and is designed to assess whole body administration of MRG-106. The first group, or cohort, of patients in Part B started receiving doses of MRG-106 in August 2016 as a subcutaneous injection of 300 mg/dose for four weeks. The next two cohorts of three patients each received injections of 600 mg or 900 mg/doses of MRG-106. One patient in the 900 mg dose cohort was withdrawn from the trial due to disease progression. Later cohorts will be dosed intravenously and dose escalation is planned to occur adaptively in increments from 100 mg to 300 mg, depending on the safety results of the drug in prior cohorts. In addition, some patients may receive the drug by a combination of routes, including subcutaneous, intravenous or intratumoral. Based on safety and tolerability, the cohort sizes may be increased to up to 10 patients. In addition to safety, tolerability and pharmacokinetics, exploratory pharmacodynamic endpoint assessments and clinical scoring using CAILS and mSWAT is being performed.

Safety, Pharmacokinetics and Pharmacodynamics

As of the end of 2016, 15 MF patients have been treated with MRG-106. MRG-106 was generally safe and well tolerated in patients at all dose levels tested, with no significant injection site reactions. Two patients did not receive all the scheduled treatments due to disease progression. No drug-related serious adverse events have been reported.

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Six patients in Part A were administered MRG-106 intratumorally, with up to five 75 mg doses of MRG-106 administered to the same tumor over a period of up to two weeks. Four of these patients were simultaneously treated in a second lesion with a saline placebo solution. All patients who received MRG-106 generally tolerated the administrations well with only minimal redness, or erythema, at the site of injection noted in one patient. One patient was discontinued from the trial after receiving three doses of MRG-106 due to rapid progression of disease, which began shortly before the initiation of dosing and was considered unrelated to MRG-106. The remaining five patients have completed the dosing and follow-up periods. Adverse events for these patients noted by the treating physician as possibly or definitely related to MRG-106, included erythema, itchiness, pain, burning or tingling at the injection site, nausea, skin inflammation and a hand sore. All possibly or definitely related adverse events were judged as mild or moderate in severity. Abnormal lab values possibly related to use of the product candidate were observed in two patients and included moderately decreased white blood cell count and neutropenia, both of which resolved while continuing MRG-106, and prolonged partial thromboplastin time.

In Part B of the clinical trial, three patients each in the 300 mg, 600 mg, and 900 mg cohorts were to receive a total of six subcutaneous doses of MRG-106 administered over a 26-day period. All three dose levels were generally well tolerated in the eight patients that completed dosing. The treating physicians for these patients noted the following adverse events, which were possibly or definitely related to MRG-106: (i) four patients experienced mild to moderate pain at the site of injections on five total occasions, (ii) one patient experienced purpura, or a rash, at an injection site, (iii) one patient experienced tenderness and bruising at injection sites, as well as intermittent blurred vision; and (iv) one patient experienced erythema around an injection site. One patient in the 900 mg dose cohort had progressive disease associated with itching, which changed from mild to severe after receiving three doses of 900 mg. This patient stopped receiving MRG-106 and was treated with prednisone, and the patient s symptoms improved. No serious adverse events have been reported in Part B. Abnormal lab values possibly related to the administration of MRG-106 included mild, transient increases in liver enzymes and creatine kinase (an indicator of muscle stress) for a single patient dosed at the 600 mg dose level and transient neutropenia in two patients dosed at the 900 mg dose level (concluded to be temporally related to treatment with gemcitabine for one patient). The change in these lab values was transient during the course of the dosing and returned to normal by the end of the dosing period. In addition, one patient in the 300 mg cohort experienced increases in liver function tests prior to dosing, which decreased during dosing and increased again to the pre-dosing levels at the measurement 30-days post-dosing.

Pharmacokinetic analysis of the plasma collected from Part A of the clinical trial indicated that MRG-106 was quickly absorbed into the systemic circulation with the highest concentrations being observed 10 minutes to one hour after MRG-106 administration. Preliminary pharmacokinetic data from Part B of the clinical trial in the first three patients dosed subcutaneously with 300 mg MRG-106 demonstrate this route of administration increases the time required to reach maximal concentrations of drug in the systemic circulation (approximately 3 hours) compared to intratumoral administration.

In Part A of the clinical trial, high levels of MRG-106 (48 -204 µg per gram of tissue) were detected in injected tumors. Miragen also observed accumulation of MRG-106 in lesions distant from the site of injection at low levels (4 µg per gram of tissue). Preliminary analysis of injected tumors also indicated an increased expression of several direct targets of miR-155, suggesting that the drug is inhibiting its intended molecular target. Biopsies were not collected in Part B patients and therefore, the pharmacodynamic effect of MRG-106 in skin lesions was not assessed.

Efficacy

All patients who received MRG-106 in Part A of the clinical trial demonstrated a beneficial clinical response. Exploratory assessment of clinical response to therapy was performed for both MRG-106-treated and saline-treated lesions based on the change from baseline in the CAILS scores. Four of the five patients who completed dosing had

their scores evaluated in the MRG-106 treated lesions. In the fifth patient, CAILS scores were monitored in two untreated lesions, instead of the treated lesions. The lesions in these four patients showed a

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50% or greater reduction in the baseline CAILS score, which was maintained to the end of study visit (either 28 days or 35 days after the first dose). In contrast, a greater than 50% reduction was observed in only one saline treated lesion. The CAILS scores for patients in Part A of the clinical trial are set forth below.

Part A: Lesion CAILS

				MRG-106 Treated Lesions			Untreated or Saline Treated Lesions		
Patient Number	Number of Doses	Dose	Duration of Treatment (Days)	First CAILS Score	Lowest CAILS Score	Maximal % Reduction in CAILS	First CAILS Score	Lowest CAILS Score	Maximal % Reduction in CAILS
1 (early termination)	3	75mg	9	18	12	33%	18	14	22%
2	4	75mg	8	16	8	50%	NA	NA	NA
3	4	75mg	8	12	6	50%	8	5	37%
4 Lesion 1	4	75mg	8	NA	NA	NA	15	8	47%
4 Lesion 2	4	75mg	8	NA	NA	NA	36	25	31%
5	5	75mg	15	26	6	77%	20	5	75%
6	5	75mg	15	12	4	67%	9	5	44%

Histological examination of pre-treatment and post-treatment tumor biopsies of the same lesion injected with MRG-106 was conducted in five patients. At baseline, these biopsies typically showed evidence of cancer and high cancer cell density. After treatment, histology revealed fewer cancerous cells or a reduction in cancer cell density or depth in most patients. One patient who received MRG-106 injections in a small tumor showed a complete absence of cancerous T-cells in the post-treatment biopsy. Another patient had a lower percentage of CD30+ large atypical cells after MRG-106 treatment, which is indicative of a reduction in the number of cells with malignant characteristics.

Part B of the clinical trial has enrolled nine patients, three in each of the 300 mg, 600 mg and 900 mg dose level cohorts, eight of whom received six doses of MRG-106 over a 26-day period. No serious adverse events have been reported in Part B. As noted above, one patient in the 900 mg dose cohort experienced disease progression and discontinued treatment. Patients in the 300 mg and 600 mg dose cohorts have completed the clinical trial, including a follow-up visit on or about the 56th day of the clinical trial. Patients in the 900 mg dose cohort are still participating in the clinical trial and are in the 30-day follow-up period.

Exploratory assessment of clinical response to therapy in Part B was performed by assessing the CAILS score for up to five lesions for each patient (one patient had only one lesion). The mSWAT and CAILS scores for each patient are shown in the table below. Because the patients who receive 900 mg doses of MRG-106 have not yet completed all assessments, the maximal reduction in mSWAT and CAILS scores are not yet available for these patients. Two patients from the 300 mg dose group demonstrated reductions in their baseline mSWAT of 50% or greater and one patient had a 75% reduction in the combined CAILS score. The reductions in both these patients were maintained to the end of study visit (56 days after the first dose). One patient in the 600 mg dose cohort showed a 53% reduction in the combined CAILS score and a 39% reduction in the overall mSWAT.

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Part B: CAILS and mSWAT

				Combined CAILS Score			mSWAT Score		
Patient Number	Number of Doses	Dose	Duration of Treatment (Days)	First CAILS Score	Lowest CAILS Score	Maximal % Reduction in CAILS	First mSWAT Score	Lowest mSWAT Score	Maximal % Reduction in mSWAT
1	6	300 mg	26	10	9	10%	2	1	50%
2	6	300 mg	26	40	10	75%	47	23	51%
3	6	300 mg	26	44	40	9%	1.5	1.1	27%
4	6	600 mg	26	45	21	53%	22	13.5	39%
5	6	600 mg	26	58	49	16%	20.3	18.8	7%
6	6	600 mg	26	82	70	15%	42.7	40.1	6%
7	6	900 mg	26	68	*	*	17.2	*	*
8	6	900 mg	26	18	*	*	5.75	*	*
9	3	900 mg	5	30	*	*	103	*	*

* Only partial data is available for patients in the 900 mg dose cohort. Patient 7 showed a 1% increase in the CAILS score on day 17 of the trial and a 28% increase in the mSWAT from baseline values on day 25 of the trial. Patient 8 showed a 22% increase in the CAILS score and a 9% increase in the mSWAT from baseline values on day 18 of the trial. Patient 9 only received three doses due to disease progression and CAILS and mSWAT scores are not yet available.

Biomarker Analysis

Biomarkers were analyzed to assess the ability of MRG-106 to regulate the expression of gene pathways that are associated with elevated levels of miR-155 in MF. Miragen identified a set of biomarkers based on MRG-106 activity in cell lines derived from MF patients. In Part A of the clinical trial, Miragen assessed the expression of these biomarker genes in lesions before and after treatment with MRG-106. Retrospective analysis of a subset of the genes from the cell line data demonstrated that MRG-106 treatment decreased expression of some genes associated with cellular proliferation and increased expression of some genes associated with cell death. The expression of these genes appears to correspond to the level of drug measured in the lesion biopsy. Miragen also believes these data illustrate the potential of its approach to identify molecular biomarkers that translate from pre-clinical studies to predict product candidate activity in clinical trials.

MRG-201

MRG-201 is a replacement for miR-29 that is intended to increase miR-29-like activity in the setting of fibrotic disease. Miragen is currently studying MRG-201 in a single-center, Phase 1, double-blind, placebo-controlled, single and multiple dose-escalation clinical trial enrolling up to 70 healthy volunteers.

Miragen believes that the miR-29 family of miRNAs is consistently present at abnormally low levels during fibrotic disease progression. Miragen initially discovered the role of miR-29 in pathological cardiac fibrosis. Since this initial discovery, miR-29 has been implicated in pathological fibrosis in multiple organs including the skin, eye, lung, liver

and kidney. miR-29 is understood by the scientific community to play a role in the regulation of certain processes that contribute to fibrosis, including the initiation and maintenance of fibrosis through transforming growth factor beta, or TGF-ß, signaling and the deposition of the components that make up fibrotic tissue, including collagen and extracellular matrix, or ECM, proteins. Furthermore, both fibrotic ECM and TGF-ß are believed to down-regulate miR-29 levels, leading to continuously increased TGF-ß expression and uncontrolled ECM production. miR-29 levels are abnormally low in multiple fibrotic indications, and lower levels of miR-29 are correlated with increased severity of fibrosis. Although various fibrotic indications are potentially distinct, they share a number of features, including the activation of the cells that initiate the deposition of fibrotic tissue or fibroblast activation, excessive deposition of collagen and other fibrosis-associated pathways, and resulting organ dysfunction. Miragen believes the functions and biomarkers regulated by miR-29 might be shared among multiple fibrotic indications and increasing miR-29-like activity may provide potential benefit in any of these.

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To demonstrate mechanistic proof-of-concept and as a potential initial indication, Miragen is initially focused on skin fibrosis. Miragen believes the data derived from skin fibrosis trials may facilitate development of a product candidate intended for the treatment for Idiopathic Pulmonary Fibrosis, or IPF, and other major organ pathological fibrosis.

There are three primary objectives that Miragen intends to address prior to potentially initiating a trial in a major organ fibrosis disease, such as lung or liver fibrosis;

Demonstrate mechanistic proof of concept in humans for MRG-201. In Miragen s Phase 1 clinical trial of MRG-201, skin fibrosis was induced by making incisions in the volunteers skin and biomarkers of fibrosis, including collagens and other fibrosis-associated genes were monitored to measure active gene regulation by MRG-201. Skin manifestation of pathological fibrosis, such as keloids that are abnormal proliferation of scar tissue that can form at the site of a skin injury and other forms of raised or hypertrophic scarring, may be an area in which Miragen conducts additional development work, depending on the data from the Phase 1 clinical trial.

Demonstrate the correlation of biological pathways between skin fibrosis and other major organ fibrosis. Miragen has identified a subset of biomarker genes that it believes are regulated by MRG-201 in pre-clinical models of skin fibrosis, including mouse, rat, and rabbit, as well as in human skin fibroblasts in culture. This subset of biomarker genes includes multiple collagens and additional fibrosis-associated genes that appear to be implicated in fibrosis. The expression of these genes is generally increased in pathological fibrosis in humans, including skin fibrosis (an example of which is scleroderma) and pulmonary fibrosis (an example of which is IPF or systemic sclerosis). This gene signature appears to be regulated in common in skin fibrosis and IPF.

Develop strategies for delivery of miR-29 replacements to allow for treatment of the lung and other major organs. Miragen is collaborating with the Lovelace Respiratory Research Institute and a laboratory at Yale University under a grant from NIH to evaluate and develop potential inhaled delivery of MRG-201. Inhaled delivery has the potential to deliver more active drug to the tissue of interest which in this case is the lung. In pre-clinical models, Miragen delivered MRG-201 to the lung and demonstrated reversal of pulmonary fibrosis in rodents which was induced by the administration of bleomycin, a chemotherapy agent known to induce lung fibrosis. In addition, MRG-201 was able to reduce pulmonary fibrosis that was induced in rodents by TGF-ß over-expression. Furthermore, a recently published study demonstrated the ability to reverse liver fibrosis in rodents through the use of an engineered virus that expresses miR-29. The viral expression of miR-29 in the study occurred in the chief functional cells of the liver. Miragen has shown in pre-clinical testing that miR-29 replacements, delivered using two different methods reduced the expression of biomarkers of fibrosis in the post-exposure animal model of liver fibrosis induced by carbon tetrachloride. Finally, Miragen believes injecting a miR-29 mimic into the eye may allow for a local administration for reduction of retinal fibrosis.

Pathological Fibrosis

Fibrosis describes the development of fibrous connective tissue as a response to injury or damage. Fibrosis may refer to the deposition of connective tissue that occurs as part of normal healing or to the excess tissue deposition that occurs as a disease process. When fibrosis occurs in response to injury, the term scarring is used. Pathological fibrosis can occur in many tissues of the body as a result of inflammation or damage. In pathological fibrosis, collagen build

up occurs, which can result in scarring of vital organs such as the skin, lung, liver, eye, kidney and heart leading to irreparable damage and eventual organ failure. Miragen believes there is a significant need for additional clinically satisfactory therapeutic approaches to treating pathological fibrosis.

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Below is a description of several types of pathological fibrosis that Miragen may seek to develop a product candidate based on a replacement for miR-29:

Type of Pathological Fibrosis	Description
Skin Fibrosis	Scarring is a result of an over production of collagen in a healing wound. Scarring may continue to thicken for up to six months or may overgrow the site of the wound, even after the wound has healed.
	Hypertrophic scars and keloids are abnormal wound responses, and represent an excessive connective tissue response to skin trauma, inflammation, surgery, or burns.
	Hypertrophic scars and keloids are characterized by local fibroblast proliferation and overproduction of collagen. Both hypertrophic scars and keloids are diseases that tend to be painful and itchy, restrict mobility, and are resistant to treatment.
Pulmonary Fibrosis	Pulmonary fibrosis, also known as lung fibrosis, refers to a number of conditions that cause lung damage in the tissue between and supporting the air sacs or interstitial tissue, followed by fibrosis and eventually loss of lung elasticity. These conditions lead to symptoms such as persistent cough, chest pain, difficulty breathing and fatigue. Pulmonary fibrosis may occur as a secondary condition in various other diseases, but in many cases the underlying cause is not clear, and is referred to as IPF.
	IPF is a chronic, progressive lung disease which ultimately leads to death in many of the patients. This condition causes scar tissue to build up in the lungs, which makes the lungs unable to transport oxygen into the bloodstream effectively.
Liver Fibrosis	Liver fibrosis refers to the scar tissue and nodules that replace liver tissue and disrupt liver function. Major causes of liver fibrosis are alcohol, chronic hepatitis B virus, hepatitis C virus infection along with the metabolic disorders non-alcoholic fatty liver disease and non-alcoholic steatohepatitis. Liver fibrosis is a major global problem driven by increasing rates of obesity and diabetes.
Eye Fibrosis	Infection or inflammation of the eye results in impairment of visual function. Chronic inflammation can ultimately lead to fibrosis.

Eye fibrosis diseases include retinal fibrosis such as diabetic retinopathy and proliferative vitreoretinopathy, corneal fibrosis, glaucoma trabeculectomy, age related macular degeneration, and Fuch s endothelial corneal dystrophy.

MRG-201 Phase 1 Clinical Trial

Trial Design

Miragen is conducting a single-center Phase 1, double-blind, placebo-controlled, single and multiple dose-escalation clinical trial of MRG-201. MRG-201 is designed to mimic the activity of a molecule called miR-29 that has been shown to decrease the expression of collagen and other proteins that are involved in scar formation. MRG-201 is being studied to determine if it can limit the formation of fibrous scar tissue that leads to pathologic fibrosis. This four-part clinical trial is expected to enroll up to 70 healthy volunteers in which:

Part A studied the expression of biomarker genes in skin at different time points following an incision, and was performed without product candidate administration;

Part B studied a single ascending dose of 0.5 to 14 mg of MRG-201 in intact skin;

Part C studied a single ascending dose of 4, 7 or 14mg of MRG-201 administered around skin incisions; and

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Part D is studying multiple ascending doses of MRG-201 ranging from 4 mg to 14 mg administered around skin incisions.

The primary objectives in this clinical trial are safety and tolerability of MRG-201 injected into the skin via intradermal injections. A secondary objective is to characterize local skin and systemic exposure to MRG-201 following intradermal injection. Exploratory endpoints include the pharmacodynamic effects of MRG-201 on the expression of miR-29 gene targets in skin wound biopsies and to evaluate changes in histology from skin wounds treated with MRG-201.

Safety and Pharmacokinetics

As of the end of 2016, 47 volunteers have participated in the clinical trial, 40 of whom have been administered MRG-201 and seven of whom were incised without receiving a dose of MRG-201.

Nineteen volunteers in Part B received a single dose of 0.5 mg, 1 mg, 2 mg, 4 mg, 7 mg or 14 mg of MRG-201 in unincised skin. In these volunteers, MRG-201 was generally well tolerated. Three incidents of injection site reactions were reported, which were generally moderate. Three additional adverse events of mild severity were reported as possibly related to receiving MRG-201, and included erythema and sensation of warmth on limbs and back, both of which resolved within 24 hours, as well as fatigue which resolved by day seven.

Nine volunteers in Part C received a single dose of either 4 mg, 7 mg or 14 mg MRG-201 around an incision (three volunteers per group). In these volunteers, MRG-201 was generally well tolerated at all dose levels evaluated. One incident of injection site reaction was reported, which was moderate and resolved within 48 hours.

Nine volunteers in the dose-escalation portion of Part D received six total doses each of 4 mg, 7 mg or 14 mg MRG-201 around an incision. In these volunteers, MRG-201 was generally well tolerated at all dose levels evaluated. There were two injection site reactions of moderate severity reported. Five adverse events of mild severity reported by the treating physicians as possibly or definitely related to receiving MRG-201 included itching or pain at the injection site, fatigue, headache, and microscopic hematuria (blood in the urine), which had all resolved by the end of the study.

An additional three volunteers were enrolled in Part D to understand drug diffusion. Subjects received six total doses each of 14 mg MRG-201 at one end of a 4 cm incision. The other end of the incision is untreated. Both ends of the incision will be biopsied to measure the potential for diffusion and pharmacodynamic activity of MRG-201 away from the site of injection. In these volunteers, MRG-201 was generally well tolerated at all dose levels evaluated. One volunteer had an injection site reaction of moderate severity.

Preliminary pharmacokinetic analysis of plasma collected from the MRG-201 volunteers in Part B, Part C, and Part D (data available for 4 mg cohort only) of the clinical trial revealed that very little drug (less than 100 ng/mL) is generally detectable in the blood when MRG-201 is injected intradermally into the skin.

Biomarker Analysis

In Part A of the clinical trial in which volunteers were incised without receiving any product candidate or placebo, molecular analysis confirmed that miR-29 expression decreased in incised skin compared to unincised skin, as expected for fibrosis. In addition, gene expression of miR-29/MRG-201 biomarkers, including collagens and fibrosis-related genes, was increased approximately two-to-20-fold in incised skin, and was correlated with the decrease in miR-29 expression. The magnitude of the change in the expression of miR-29 and the biomarker genes was ~30-85% greater 16 days after administration than it was nine days after administration, indicating a time-dependent effect on gene expression. Miragen believes these data indicate the role of miR-29 in potentially

regulating the biological pathways implicated in fibrosis in human skin.

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In Part C of the clinical trial, biomarkers were analyzed to assess the ability of MRG-201 to regulate the expression of genes that are associated with reduced miR-29 expression in human skin. Miragen identified a set of biomarkers based on MRG-201 activity in pre-clinical models of skin fibrosis, including mouse, rat, and rabbit skin *in vivo*, as well as human skin fibroblasts *in vitro*. The biomarker panel consists of direct targets for miR-29 and downstream genes Miragen believes are indicative of an impact on miR-29 expression in wound healing and fibrosis, particularly collagens and other genes important in fibrosis. Miragen assessed the expression of these biomarkers in biopsies taken from the site of the incision 24 hours after a single MRG-201 dose compared to saline-treated lesions. Analysis of the biomarker data indicated that MRG-201 decreased expression of collagens and fibrosis-associated genes, consistent with the role Miragen believes miR-29 plays in regulating these fibrosis-related genes. The change in expression of collagens and fibrosis-related genes appeared to be correlated with the amount of MRG-201 administered. Miragen believes these data demonstrate an effect of MRG-201 on fibrosis-associated genes, and provide an indication that MRG-201 has the potential to reduce fibrosis and scar formation in human skin. Miragen also believes these data highlight the potential of its approach to identify molecular biomarkers that translate from pre-clinical studies to assessing the activity of MRG-201 in human clinical trials.

Part D of the clinical trial is currently in progress. Four cohorts of three volunteers each received six total doses of 4 mg, 7 mg or 14 mg MRG-201 and have completed dosing and the follow-up process. Based on biomarker analysis, the collagen and fibrosis-related genes were decreased in four of the six drug-treated incisions compared to the saline control that have been analyzed to date. Additionally, preliminary histological analysis indicated that incisions treated with multiple administrations of MRG-201 showed a reduction in the area and depth of fibroplasia, a marker of fibrosis or scar formation. Miragen believes these data may suggest that MRG-201 has the potential to reduce fibrosis and scar formation in human skin. The collagens and extracellular matrix genes regulated by MRG-201 in human skin have also been implicated in pulmonary fibrosis, including IPF. Miragen believes the molecular and histological data for MRG-201 in human skin support additional development of a miR-29 mimic for IPF and additional fibrotic indications.

Histopathology

Biopsies taken on day 16 from MRG-201 or saline treated incisions were assessed by a pathologist for the depth, width and overall area of fibroplasia. Histological analysis of the first nine volunteers biopsies in Part D indicated that incisions treated with multiple administrations of MRG-201 generally showed a reduction in the area and depth of fibroplasia. Miragen believes an effect of MRG-201 on fibroplasia during normal wound healing to be potentially predictive of a treatment effect for a replacement for miR-29 in excessive fibrotic diseases. Miragen believes these data suggest that MRG-201 may be able to reduce pathological fibrosis and scar formation in human skin.

MRG-201 Pre-Clinical Activities

Correlation of Biological Pathways Between Skin Fibrosis and Other Major Organ Fibrosis

The biomarkers that Miragen believes are regulated by MRG-201 in human skin represent biological pathways that are associated with skin fibrosis, but are also fundamental processes involved in pathologic fibrosis in general. Increased expression of collagens and additional fibrosis-associated genes that Miragen believes are down-regulated by MRG-201 have been associated with multiple fibrotic indications, including scleroderma, keloids, hypertrophic scarring, IPF, systemic sclerosis, pulmonary fibrosis, fibrosis of the eye (retinal and corneal fibrosis), kidney fibrosis, and cardiac fibrosis. Miragen believes the potential ability of MRG-201 to reduce the expression of these fibrosis-associated biomarkers in human skin suggests that a miR-29 mimic could also provide anti-fibrotic activity in multiple fibrotic indications.

Work done by Miragen, as well as published data indicate that a set of biomarkers showing increased expression in response to incision-induced fibrosis in human skin also show increased expression in multiple fibrotic indications including pulmonary fibrosis.

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Delivery of miR-29 Mimic to the Lung

Together with Yale University and Lovelace Respiratory Research Institute, Miragen was awarded a Centers for Advanced Diagnostics and Experimental Therapeutics in Lung Disease Stage II Grant from the NIH in 2014. The objective of the grant is to develop miR-29 mimicry as an efficient and personalized anti-fibrotic therapy. The collaboration is currently in year three of the five-year grant. During the first two years of the grant, the group compared intravenous and aerosolized delivery routes for the amount of miR-29 mimic that enters circulation, distribution, pharmacokinetics, pharmacodynamics, and efficacy. In one of its laboratories, Yale University also established a blood assay for miR-29 detection in IPF patients. During years three through five of the grant, Miragen plans to perform potential IND-enabling activities including additional development of an aerosolized formulation and dose of miR-29 mimic, good manufacturing practice, or GMP, manufacturing of the product candidate, and complete good laboratory practice, or GLP, toxicology studies. In addition, the collaboration plans to further develop its blood miR-29 diagnostic and assess correlations to tissue and lung cells collected through a procedure called bronchoalveolar lavage.

Delivery of miR-29 Mimic to the Liver

miR-29 family members are expressed at less than normal levels in pre-clinical models of liver fibrosis as well as in biopsies from human fibrotic livers. Delivery of miR-29 to liver cells using Adeno-Associated Virus, or AAV, has been shown to reverse liver fibrosis induced by carbon tetrachloride in a rodent model. Miragen is currently assessing liver delivery of several miR-29 replacements with varying conjugates. Initial data from such assessments has shown liver delivery in rodent models. Miragen is studying multiple compounds in an efficacy study in rodents with the AAV-delivered miR-29 in a carbon tetrachloride model of liver fibrosis. Miragen believes the results of these studies will assist Miragen s potential compound selection for IND-enabling activities with novel miR-29 replacements or the use of AAV for the delivery of miR-29 in hepatic fibrosis.

Delivery of miR-29 Mimic to the Eye

Miragen is exploring miR-29 as a therapeutic for ocular indications including ocular fibrosis. RNA-based therapeutics can be administered to the eye via eye drops for diseases affecting the front of the eye (e.g., the cornea and anterior chamber), and via injection into the eye for diseases affecting the back of the eye (which is commonly referred to as the retina). Both routes of administration have been established to be generally well-tolerated for oligonucleotide therapeutics. Miragen believes that the direct application of Miragen s microRNA therapeutic candidate to the eye may have the advantage of a greater than one-week duration, as the posterior chamber of the eye is a closed compartment, and is devoid of the usual clearance mechanisms present in the rest of the body. Historically, this mode of drug delivery potentially allows infrequent dosing, and also provides the potential advantage of reduced systemic exposure. Preliminary pre-clinical studies investigated direct injection into the eye of a double-stranded RNA molecule structurally similar to the design of MRG-201, and demonstrated decreased expression of the targeted gene. These data demonstrated functional delivery of double-stranded RNA molecules to the retina in the absence of a delivery vehicle.

Cardiovascular Disease

Miragen is also developing RNA therapeutics in three cardiovascular programs through Miragen s collaboration with Servier. Under this collaboration, Miragen granted Servier exclusive licenses to three cardiovascular product candidates. Servier may fund development through Phase 2 clinical trials, while Miragen retains all commercial rights to these programs in the United States and Japan.

Miragen has additional pre-clinical cardiovascular programs in which it is collaborating with academic institutions. In 2015 Miragen was designated as a collaborating institution for a grant that provides more than 2 million over a three-year period (2015-2017) funded by the German Federal Ministry of Education and Research.

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Other Pre-Clinical Programs

In 2016, Miragen was awarded a milestone-driven grant by The ALS Association of up to $0.4 million to advance the development of MRG-107. MRG-107 is an inhibitor of miR-155 intended to be developed for the treatment of amyotrophic lateral sclerosis, or ALS.

Miragen is also evaluating and developing additional microRNA-targeted, pre-clinical product candidates in a variety of disease indications where an abnormal level of one or more microRNAs has been implicated in disease pathology. Miragen s inhibitor programs, including these product candidates, were created using the locked nucleic acid technology that Miragen exclusively licensed from Santaris Pharma A/S (now a wholly-owned subsidiary of Roche), on a target-by-target basis. Miragen believes combining this technology with Miragen s internal expertise may allow it to create unique product candidates that possess desirable drug-like properties capable of entering diseased cells without the need for additional delivery technologies. Miragen has a broad patent portfolio intended to protect these product candidates.

Background on microRNA

microRNAs are transcribed from the genome and unlike messenger RNA, or mRNA, they do not encode proteins. microRNAs function by preventing the translation of mRNAs into proteins and/or by triggering degradation of these mRNAs. Studies have shown that microRNA gene regulation is often not a decisive on and off switch but a subtle function that fine-tunes cellular phenotypes that becomes more pronounced during stress or disease conditions. microRNAs were first discovered in 1993 and have since been found in nearly every biological system examined since that time. They are highly conserved across species, demonstrating their importance to biological functions and cellular processes. According to the Sanger Institute, over 1,000 microRNAs have been identified in humans.

A body of evidence has shown that inappropriate levels of particular microRNAs are directly linked to a range of serious diseases, many of which are poorly served by existing therapies. microRNAs can affect the balance of protein expression and serve as command and control nodes that directly coordinate multiple critical systems simultaneously. This effect on systems biology is a naturally occurring homeostatic process that becomes disrupted in certain disease states. As a result, developing microRNA therapeutics is fundamentally different from the single-protein, single-target approach that is the foundation of traditional small and large molecule drugs.

Miragen s Approach to Drug Discovery and Development

Miragen believes that its drug discovery and development strategy will enable it to progress its product candidates from pre-clinical discovery to achievement of a plausible link to clinical benefit in humans relatively quickly and efficiently.

Discovery

Although there are over 1,000 identified human microRNAs, not all of them have been shown to be causal in disease. Miragen s approach to drug discovery and development begins with the identification of potentially pathological microRNAs.

Miragen applies three general approaches to the identification of potentially pathological, or disease causing, microRNAs (i) profiling of microRNA expression in diseased tissue versus normal tissue to identify microRNAs that are found at abnormally high or low levels (ii) identification of microRNAs that are located within genes (typically in non-protein coding segments) of validated disease relevant genes and thus simultaneously expressed with the disease

associated gene and (iii) evaluation of microRNAs that are predicted to directly modulate the expression of specific disease relevant genes.

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Miragen has biased its programs to develop therapeutic microRNA inhibitors as opposed to microRNA replacements. Miragen believes the inhibitor candidates face lower delivery hurdles and have better drug-like properties in regards to affinity to their target, stability, drug distribution and pharmacodynamics. To improve their therapeutic potential, Miragen chemically modifies these compounds with changes such as locked nucleic acid (known as LNA) substitution of the ribose sugar in many of the nucleosides and deoxyribonucleoside (known as DNA).

In conditions where a deficit in microRNA expression has been identified as disease causing, microRNA replacements, which are modified double-stranded RNA structures that are recognized by the RNA-induced silencing complex, or RISC, can serve as chemically synthesized replacements for microRNAs.

Historically, the delivery of double stranded RNA s, such as microRNA replacements, has been a significant hurdle to overcome for drug development because these molecules are very rapidly degraded, and because uptake into cells can be inefficient. Miragen s delivery approach for microRNA replacements is to append a conjugate to the molecule to enhance cellular uptake. The selection of the conjugate is dependent on the intended therapeutic use. Miragen has deployed hydrophobic conjugates, such as cholesterol that are able to improve pharmacokinetics and allow for enhanced cellular uptake. Miragen is also exploring a range of conjugates that help in targeting specific tissues and cells. Miragen s strategy with microRNA replacements has centered on opportunities for efficient delivery of the molecules with an emphasis on local and topical applications, such as injections in the skin or lung, respectively. For organs where topical or local applications are not feasible, such as the liver, Miragen has employed conjugates that have demonstrated successful delivery after systemic administration.

Development

Miragen s approach to translational medicine is focused on rapidly testing the molecular hypothesis in human cell lines and animal models to demonstrate safety, pharmacokinetics, and pharmacodynamics, and finally designing and conducting small, efficient and targeted human Phase 1 clinical trials. Miragen typically selects an initial indication that is genetically defined or is a rare disease where abnormal levels of a microRNA have been implicated. These early stage Phase 1 clinical trials are designed to test the mechanistic relevance or develop mechanistic proof-of-concept in humans in a setting that provides the opportunity to develop a biomarker toolkit for a mechanism of action that Miragen believes has broader disease relevance.

The mechanistic proof-of-concept studies are designed to provide relevant information that helps to reduce development risks in humans. Miragen s aim is to demonstrate that the expression levels of the microRNA could potentially serve as a diagnostic indicator that allows for better patient selection for later clinical trials and in additional indications. At the same time, Miragen seeks to confirm molecular activity of the drug.

By measuring the pharmacodynamics of target engagement, Miragen is able to show that the product candidate effectively enters the appropriate cell and binds to its intended target. This process is particularly important for oligonucleotide drugs. Miragen can also measure the effects on a series of downstream genes that create a plausible link between target engagement and a mechanism of disease.

For some diseases, Miragen believes that local administration allows it to achieve a variety of concentrations of drug at the site of action and facilitates the development of dose / response relationships. Miragen believes understanding the dose necessary to show target engagement, with concomitant surrogate marker alterations provides the basis for which a systemic dose can be defined that will be necessary to potentially achieve a therapeutic effect.

Exploratory endpoints can provide Miragen with verification of the pharmacodynamic effects of the drug based on biomarker readouts and morphological alterations. This translational strategy allows Miragen to answer many

questions about the drug target pair and provides improved confidence that the molecular basis of drug action is

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relevant in humans. Having built confidence in the drug mechanism and demonstrated an acceptable safety profile, later stage clinical trials will be designed to establish appropriate dose and therapeutic efficacy.

Miragen s Strategic Collaborations and License Agreements

Strategic Alliance and Collaboration with Servier

In October 2011, Miragen entered into the Servier Collaboration Agreement with Servier for the research, development, and commercialization of RNA-targeting therapeutics in cardiovascular disease, which was subsequently amended in May 2013, May 2014, May 2015 and September 2016. Under the Servier Collaboration Agreement, Miragen granted Servier an exclusive license to research, develop, and commercialize RNA-targeting therapeutics for three targets in the cardiovascular field. As of December 31, 2016, three named targets exist under the Servier Collaboration Agreement, two of which are replaceable by Servier.

Servier s rights to each of the targets are limited to therapeutics in the cardiovascular field in their territory, which is worldwide except for the United States and Japan. Miragen retains all rights for each named target in the United States and Japan and for any products or product candidates outside of the cardiovascular field.

In connection with entering into the strategic alliance with Servier, Miragen received a nonrefundable upfront payment of $8.4 million (6.0 million) in 2011 and an additional $4.0 million (3.0 million) in 2013 when Servier exercised their right to name a third target under the agreement. Miragen is also eligible to receive development milestone payments of 5.8 million to 13.8 million ($6.5 million to $15.5 million as of September 30, 2016) and regulatory milestone payments of 10.0 million to 40.0 million ($11.2 million to $44.8 million as of September 30, 2016) for each target. Additionally, Miragen may receive up to 175 million ($196 million as of September 30, 2016) in commercialization milestones as well as quarterly royalty payments between the low-double digits to the mid-teens (subject to reductions for patent expiration, generic competition, third-party royalty and costs of goods) on the net sales of any licensed product commercialized by Servier. Additionally, if Miragen undergoes a change of control in specified circumstances, Servier has agreed to increase this royalty by an additional percentage in the low-single digits if it seeks to use any of the acquiror s intellectual property in the development of product candidates under the Servier Collaboration Agreement. Servier is obligated to make any such royalty payment for a specified period under the Servier Collaboration Agreement.

As part of the Servier Collaboration Agreement, Miragen established a multiple-year research collaboration, under which Miragen jointly performs agreed upon research activities directed to the identification and characterization of named targets and oligonucleotides in the cardiovascular field, which Miragen refers to as the Research Collaboration. The initial three-year term of the Research Collaboration was extended by two additional years in May 2014 and again by one additional year in September 2016 through October 2017. Servier is responsible for funding all of the costs of the Research Collaboration, as defined under the Servier Collaboration Agreement. During the nine months ended September 30, 2016 and 2015, Miragen recognized as revenue amounts reimbursable to Miragen under the Servier Collaboration Agreement for research and development activities of $2.1 million and $3.0 million, respectively.

The development of each product candidate (commencing with registration enabling toxicology studies) under the Servier Collaboration Agreement is performed pursuant to a mutually agreed upon development plan to be conducted by the parties as necessary to generate data useful for both parties to obtain regulatory approval of such product candidates. Servier is responsible for a specified percentage of the cost of research and development activities through the completion of one or more Phase 2 clinical trials and will reimburse Miragen for a specified portion of such costs Miragen incurs. The costs of Phase 3 clinical trials for each product candidate will be allocated between the parties at a specied percentage of costs between the parties upon the occurrence of specified events under the Servier

Colloboration Agreement, including if Miragen enters into a third-party agreement for the development and/or commercialization of a product in the United States at least 180 days before the initiation of the first Phase 3 clinical trial or if Miragen subsequently enters into a U.S. partner

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agreement or if Miragen does not enter into a U.S. partner agreement, but files for approval in the United States using data from the Phase 3 clinical trial. Miragen is responsible, by itself or through a third-party manufacturer, for the manufacture and supply of all licensed oligonucleotides during the pre-clinical phase of development under the Sevier Collaboration Agreement while Servier is primarily responsible for manufacture and supply of all licensed oligonucleotides and product during the clinical phase of development under the Servier Collaboration Agreement. The parties are each responsible for the commercial supply of any licensed product to be sold in each s respective territory under the Servier Collaboration Agreement.

Under the Servier Collaboration Agreement, Miragen also granted Servier a royalty-free, non-exclusive license to develop a companion diagnostic for any therapeutic product which may be developed by Servier under the Servier Collaboration Agreement. Miragen also granted Servier an exclusive, royalty free license to commercialize such a companion diagnostic for use in connection with such therapeutic product in its territory.

The Servier Collaboration Agreement will expire as to each underlying product candidate when Servier s royalty obligations as to such product candidate have expired. Servier may also terminate the Servier Collaboration Agreement for (i) convenience upon a specified number of days prior notice to Miragen or (ii) upon determination of a safety issue relating to development under the agreement upon a specified number of days prior notice to Miragen. Either party may terminate the Servier Collaboration Agreement upon a material breach by the other party which is not cured within a specified number of days. Miragen may also terminate the agreement if Servier challenges any of the patents licensed by Miragen to Servier.

License Agreements with the University of Texas

As of September 30, 2016, Miragen had five exclusive patent license agreements, or the UT License Agreements, with the Board of Regents of The University of Texas System, or the University of Texas. Under each of the UT License Agreements, the University of Texas granted Miragen exclusive and nonexclusive licenses to certain patent and technology rights. The University of Texas is a minority stockholder of Miragen.

In consideration of rights granted by the University of Texas, Miragen agreed to (i) pay a nonrefundable upfront license documentation fee in the amount of $10 thousand per license, (ii) pay an annual license maintenance fee in the amount of $10 thousand per license starting one year from the date of each agreement, (iii) reimburse the University of Texas for actual costs incurred in conjunction with the filing, prosecution, enforcement, and maintenance of patent rights prior to the effective date, and (iv) bear all future costs of and manage the filing, prosecution, enforcement, and maintenance of patent rights. In 2015 and 2014, Miragen incurred upfront and maintenance fees under the UT License Agreements totaling $0.1 million, and recorded the amounts as research and development expense. All costs related to the filing, prosecution, enforcement, and maintenance of patent and technology rights are recorded as general and administrative expense when incurred.

Under the terms of the UT License Agreements, Miragen may be obligated to make the following future milestone payments for each licensed product candidate: (i) up to $0.6 million upon the initiation of defined clinical trials, (ii) $2.0 million upon regulatory approval in the United States, and (iii) $0.5 million per region upon regulatory approval in other specified regions. Additionally, if Miragen successfully commercializes any product candidate subject to the UT License Agreements, Miragen is responsible for royalty payments in the low-single digits and payments up to a percentage in the mid-teens of any sublicense income, subject to specified exceptions, based upon net sales of such licensed products. UT s right to these royalty payments will expire as to each license agreement upon the expiration of the last patent claim subject to the applicable UT License Agreement.

The license term extends on a country by country basis until the expiration of the last to expire of the licensed patents that covers such product in such country. Upon expiration of the royalty payment obligation, Miragen will have a fully paid license in such country. Miragen may also terminate each UT License Agreement for convenience upon a specified number of days prior notice to the University of Texas. The University of Texas

also has the right to earlier terminate the UT License Agreements after a defined date under specified circumstances where Miragen has effectively abandoned its research and development efforts or has no sales. The UT License Agreements will terminate under customary termination provisions including Miragen s bankruptcy or insolvency, material breach, and upon mutual written consent. Miragen has expensed all charges incurred under the UT License Agreements to date, due to the uncertainty as to future economic benefit from the acquired rights.

License Agreement with Roche Innovation Center Copenhagen A/S (formerly Santaris Pharma A/S)

In June 2010, Miragen entered into a license agreement with the Santaris Pharma A/S, which subsequently changed its name to Roche Innovation Center Copenhagen A/S, or RICC, which was subsequently amended in October 2011 and amended and restated in December 2012, or the RICC License Agreement. In 2014, Santaris Pharma A/S was acquired by F. Hoffmann-La Roche Ltd, or Roche, and has become a wholly-owned subsidiary of Roche.

Under the RICC License Agreement, Miragen received exclusive and nonexclusive licenses from RICC to use specified technology of RICC, or the RICC Technology, for specified uses including research, development, and commercialization of pharmaceutical products using this technology worldwide. Under the RICC License Agreement, Miragen has the right to develop and commercialize the RICC Technology directed to four specified targets and the option to obtain exclusive product licenses for up to six additional targets. The acquisition of Santaris Pharma A/S by Roche was considered a change-of-control under the RICC License Agreement, and as such, certain terms and conditions of the RICC License Agreement changed, as contemplated and in accordance with the RICC License Agreement. These changes primarily relate to milestone payments reflected in the disclosures below. As consideration for the grant of the license and option, Miragen previously paid RICC $2.3 million and issued RICC 856,806 shares of Miragen s Series A convertible preferred stock, which are now owned by Roche Finance Ltd, an affiliate of Roche. If Miragen exercises its option to obtain additional product licenses or to replace the target families, Miragen will be required to make additional payments to RICC.

Under the terms of the RICC License Agreement, milestone payments were previously decreased by a specified percentage as a result of the change of control by RICC referenced above. Miragen is obligated to make future milestone payments for each licensed product for up to $5.2 million. Certain of these milestones will be increased by a specified percentage if Miragen undergoes a change in control during the term of the RICC License Agreement. If Miragen grants a third party a sublicense to the RICC Technology, in lieu of the fixed milestone payments noted above, Miragen is required to remit to Roche up to a specified percentage of the upfront and milestone payments Miragen receives under its sublicense.

If Miragen successfully commercializes any product candidate subject to the RICC License Agreements, then RICC is entitled to royalty payments in the mid-single digits on the net sales of such product, provided that if such net sales are made by a sublicensee under the RICC License Agreement, RICC is entitled to royalty payments equal to the lesser of a percentage in the mid-single digits on the net sales of such product or a specified percentage of the royalties paid to Miragen by such sublicensee, subject to specified restrictions. Miragen is obligated to make any such royalty payments until the later of (i) a specified anniversary of the first commercial sale of the applicable product or (ii) the expiration of the last valid patent claim licensed by RICC under the RICC License Agreement underlying such product. Upon the occurrence of specified events, the royalty owed to RICC will be decreased by a specified percentage.

The RICC License Agreement will terminate upon the latest of the expiration of all of RICC s royalty rights, the termination of the last Miragen target or the expiration of its right to obtain a product license for a new target under the RICC License Agreement. Miragen may also terminate the RICC License Agreement for convenience upon a specified number of days prior notice to RICC, subject to specified terms and conditions. Either party may terminate

the RICC License Agreement upon an uncured material breach by the other party and RICC may terminate the RICC License Agreement upon the occurrence of other specified events that are not cured within a specified number of days.

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License Agreements with the t2cure GmbH

In October 2010, Miragen entered into a license and collaboration agreement, or the t2cure Agreement, with t2cure GmbH, or t2cure, which was subsequently amended in July 2014. Under the t2cure Agreement, Miragen received a worldwide, royalty bearing, and exclusive license to specified patent and technology rights to develop and commercialize product candidates targeted at miR-92.

In consideration of rights granted by t2cure, Miragen paid a onetime upfront fee of $46 thousand and agreed to: (i) pay an annual license maintenance fee in the amount of 3 thousand ($3 thousand at September 30, 2016), and (ii) reimburse t2cure for 100% of actual costs incurred in conjunction with the filing, prosecution, enforcement, and maintenance of patent rights prior to the effective date. All costs related to the filing, prosecution, enforcement, and maintenance of patent and technology rights are recorded as general and administrative expense when incurred.

Under the terms of the t2cure Agreement, Miragen is obligated to make the following future milestone payments for each licensed product: (i) up to $0.7 million upon the initiation of certain defined clinical trials, (ii) $2.5 million upon regulatory approval in the United States and (iii) up to $1.5 million per region upon regulatory approval in the European Union or Japan. Additionally, if Miragen successfully commercializes any product candidate subject to the t2cure Agreement, Miragen is responsible for royalty payments in the low-single digits upon net sales of licensed products and sublicense fees equal to a percentage in the low-twenties of sublicensed income to Miragen. Miragen is obligated to make any such royalty payment until the later of (i) the tenth anniversary of the first commercial sale of the applicable product or (ii) the expiration of the last valid claim to a patent licensed by t2cure under the t2cure Agreement covering such product. If such patent claims expire prior to the end of the ten-year term, then the royalty owed to t2cure will be decreased by a specified percentage.

The license term extends on a country by country basis until the later of: (i) the tenth anniversary of the first commercial sale of a licensed product in a country, and (ii) the expiration of the last to expire valid claim that claims such licensed product in such country. Upon expiration of the royalty payment obligation, Miragen will have a fully paid license in such country. Miragen has the right to terminate the t2cure Agreement at will, on a country-by-country basis, after 60 days written notice.

Patent License Agreement with The Brigham and Women s Hospital

In May 2016, Miragen entered into an exclusive patent license agreement, or the BWH License Agreement, with The Brigham and Women s Hospital, or BWH.

Under the BWH License Agreement, BWH granted Miragen an exclusive, worldwide license, including a right to sublicense, to specified technology and patent rights of BWH. As consideration for this exclusive license, Miragen paid BWH a specified issue fee and is obligated to pay a specified annual license fee. BWH is also entitled to milestone payments of up to $2.6 million for any of Miragen s product candidates developed based on the patent rights subject to the BWH License Agreement plus a one-time sales milestone payment of $0.25 million for all product candidates developed based on the patent rights subject to the BWH License Agreement. If Miragen were to successfully commercialize any product candidate subject to the BWH License Agreement, then BWH is entitled to royalty payments in the low-single digits on the net sales of such product. BWH s right to these royalty payments will expire upon the expiration of the last patent claim subject to BWH License Agreement. BWH is also entitled to a percentage in the low-double digits of any sublicense income from such product, subject to specified exceptions. Miragen is also responsible for all costs associated with the preparation, filing, prosecution and maintenance of the patent rights subject to the BWH License Agreement.

Additionally, Miragen is obligated to use commercially reasonable efforts to develop a product under the BWH License Agreement and to meet specified diligence milestones thereunder.

The BWH License Agreement will terminate upon the expiration of all issued patents and patent applications subject to the patent rights under the agreement. Miragen may also terminate the BWH License Agreement for

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convenience upon a specified number of days prior notice to BWH. BWH may terminate the BWH License Agreement upon a material breach by Miragen of its payment obligations and upon the occurrence of other specified events that are not cured within a specified number of days.

Subcontract Agreement with Yale University

In October 2014, Miragen entered into a subcontract agreement, or the Yale Agreement, with Yale which was subsequently amended in February 2016 and November 2016. Under the Yale Agreement, Miragen agreed to provide specified services regarding the development of a proprietary compound that targets microRNA-29 in the indication of idiopathic pulmonary fibrosis. Yale entered into the Yale Agreement in connection with a grant that Yale received from the National Institutes of Health, or NIH, for the development a microRNA-29 mimicry as a potential therapy for pulmonary fibrosis.

In consideration of Miragen s services under the Yale Agreement, Yale has agreed to pay Miragen up to $1.1 million. Under the terms of the Yale Agreement, Miragen retains all rights to any and all intellectual property developed solely by Miragen in connection with the Yale Agreement. Yale has also agreed to provide Miragen with an exclusive option to negotiate in good faith for an exclusive, royalty-bearing license from Yale for any intellectual property developed by Yale or jointly by the parties under the Yale Agreement. Yale is responsible for filing, prosecuting and maintaining foreign and domestic patent applications and patents on all inventions jointly developed by the parties under the Yale Agreement.

The Yale Agreement terminates automatically on the date that Yale delivers its final research report to the NIH under the terms of the grant underlying the Yale Agreement. Either party may also terminate the Yale Agreement upon a specified number of days notice in the event that the NIH s grant funding is reduced or terminated or upon material breach by the other party.

Manufacturing

Miragen does not own or operate manufacturing facilities for the production of MRG-106, MRG-201 or other product candidates that Miragen develops, nor does it have plans to develop its own manufacturing operations in the foreseeable future. Miragen currently depends on third-party contract manufacturers for all of its required raw materials, active pharmaceutical ingredients, and finished product candidates for its clinical trials. Miragen does not have any current contractual arrangements for the manufacture of commercial supplies of MRG-106, MRG-201 or any other product candidates that Miragen develops. Miragen currently employs internal resources and third-party consultants to manage Miragen s manufacturing contractors.

Sales and Marketing

Miragen has not yet defined its sales, marketing or product distribution strategy for MRG-106, MRG-201 or any of Miragen s other product candidates because its product candidates are still in pre-clinical or early-stage clinical development. Miragen s commercial strategy may include the use of strategic partners, distributors, a contract sale force, or the establishment of its own commercial and specialty sales force. Miragen plans to further evaluate these alternatives as it approaches approval for one of its product candidates.

Intellectual Property

Miragen is actively building an intellectual property portfolio around Miragen s clinical-stage product candidates and discovery programs. A key component of this portfolio strategy is to seek patent protection in the United States and in

major market countries that Miragen considers important to the development of its business worldwide. As of November 16, 2016 Miragen had a portfolio of 190 patents and patent applications of which 96 are issued or allowed and 94 are pending applications. This portfolio includes methods of use and composition patents, and patent applications, on Miragen s two lead product candidates, MRG-106 and MRG-201. Miragen s

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success depends in part on Miragen s ability to obtain and maintain proprietary protection for Miragen s product candidates and other discoveries, inventions, trade secrets and know-how that are critical to Miragen s business operations. Miragen s success also depends in part on Miragen s ability to operate without infringing the proprietary rights of others, and in part, on Miragen s ability to prevent others from infringing Miragen s proprietary rights. A comprehensive discussion on risks relating to intellectual property is provided under Risk Factors under the subsection Risks Related to Miragen s Intellectual Property .

Miragen has filed composition of matter patent applications covering MRG-106 in June of 2016 in the United States as U.S. 15/173,368 and a PCT application as PCT/US2016/035865 to access foreign countries.

Miragen expects this U.S. patent will issue in the next two to three years with an expiration year of 2036 if Miragen continues to pay the maintenance fees and annuities when due, with the possibility of additional terms from the USPTO prosecution delays and from patent term extensions that may be granted due to administrative delays in the FDA. Miragen also has pending applications that cover various therapeutic uses of MRG-106. Collectively, these patents, if they issue, would have patent expirations from 2036 on if Miragen continues to pay the maintenance fees and annuities when due, not including any possible additional terms for patent term adjustments or patent term extensions. Miragen does not know if any patent will issue from any of these applications and, if any issue, Miragen does not know whether the issued patents will provide significant proprietary protection or commercial advantage against Miragen s competitors or generics. Even if they are issued, Miragen s patents may be circumvented, challenged, opposed and found to be invalid or unenforceable.

Miragen filed a composition of matter patent application covering MRG-201 in September 2015 in the United States as U.S. 14/848,085 and a PCT application PCT/US2015/49018 to access foreign countries. The U.S. patent application issued as U.S. 9,376,681 on June 28, 2016, which will expire in September of 2035 if Miragen continues to pay the maintenance fees and annuities when due, with the possibility of additional terms from USPTO prosecution delays and from patent term extensions that may be granted due to administrative delays in the FDA. Miragen also has issued patents and pending applications that cover various therapeutic uses and generic compositions of MRG-201. Collectively, these patents and patent applications, if they issue, would have patent expirations ranging from 2028 to 2035 if Miragen continues to pay the maintenance fees and annuities when due, not including any possible additional terms for patent term adjustments or patent term extensions. Miragen does not know if any patent will issue from any of the pending applications and, if any issue, Miragen does not know whether the issued patents will provide significant proprietary protection or commercial advantage against Miragen s competitors or generics. Even if they are issued, Miragen s patents may be circumvented, challenged, opposed and found to be invalid or unenforceable.

For Miragen s earlier stage product candidates, Miragen has filed compositions of matter and methods of use patent applications in the United States, under the Patent Co-operation Treaty, or the PCT, and in Argentina and Taiwan, which are not signatories to the PCT.

In addition to patent protection, Miragen seeks to rely on trade secret protection, trademark protection and know-how to expand its proprietary position around its chemistry, technology and other discoveries and inventions that Miragen consider important to Miragen s business. Miragen also seeks to protect Miragen s intellectual property in part by entering into confidentiality agreements with Miragen s employees, consultants, scientific advisors, clinical investigators and other contractors and also by requiring Miragen s employees, commercial contractors, and certain consultants and investigators, to enter into invention assignment agreements that grant it ownership of any discoveries or inventions made by them. Further, Miragen seeks trademark protection in the United States and internationally where available and when Miragen deems appropriate. Miragen has obtained registrations for the Miragen trademark, which Miragen uses in connection with Miragen s pharmaceutical research and development services as well as

Miragen s clinical-stage product candidates. Miragen currently has such registrations for Miragen in the United States, Canada and the European Union.

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Competition

The biotechnology and pharmaceutical industries are characterized by intense and rapidly changing competition to develop new technologies and proprietary products. Miragen s clinical and pre-clinical product candidates may address multiple markets. Ultimately, the diseases Miragen s product candidates target for which it may receive marketing authorization will determine Miragen s competition. Miragen believes that for most or all of its product development programs, there will be one or more competing programs under development by other companies. Any products that Miragen may commercialize will have to compete with existing therapies and new therapies that may become available in the future. Miragen faces potential competition from many different sources, including larger and better-funded biotechnology and pharmaceutical companies. In many cases, the companies with competing programs will have access to greater resources and expertise than Miragen does and may be more advanced in those programs.

Miragen believes that its current and future competition for resources and eventually for customers can be grouped into three broad categories:

- companies working to develop microRNA targeted products, including Regulus Therapeutics Inc., Mirna Therapeutics, Inc., Microlin Bio, Inc., and InteRNA Technologies B.V.;

- companies working to develop other types of oligonucleotide therapeutic products, including Ionis Pharmaceuticals, Inc., Alnylam Pharmaceuticals, Inc., Arrowhead Pharmaceuticals, Inc., Dicerna Pharmaceuticals, Inc., RaNa Therapeutics, Inc., RXi Pharmaceuticals Corporation, and Silence Therapeutics AG; and

- companies with marketed products and development programs for therapeutics that treat the same diseases for which Miragen may also be developing potential treatments.

The following companies have therapeutics marketed or in development for CTCL: Actelion Ltd, Bristol-Myers Squibb Company, Celgene Corporation, Merck & Co., Inc., Mylan Pharmaceuticals Inc., Novartis International AG, Spectrum Pharmaceuticals, Inc., Seattle Genetics, Inc., Takeda Pharmaceutical Company Ltd, and Valeant Pharmaceuticals International, Inc.

The following companies have marketed therapeutics for pulmonary fibrosis Miragen s competitors in this area include, Boehringer Ingelheim GmbH, F. Hoffmann-La Roche Ltd.

Miragen believes that the key competitive factors that will affect the success of any of its product candidates, if commercialized, are likely to be their efficacy, safety, convenience, price and the availability of reimbursement from government and other third-party payors relative to such competing products. Miragen s commercial opportunity could be reduced or eliminated if its competitors have products that are superior in one or more of these categories.

Government Regulation

FDA Drug Approval Process

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling and import and export of pharmaceutical products. Failure to comply with applicable U.S. requirements at any time during the product development process may subject a company to a variety of administrative or judicial sanctions, such as imposition of clinical hold, FDA refusal to approve pending NDAs warning or untitled letters, withdrawal of approval, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties and criminal prosecution.

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Miragen cannot market a drug product candidate in the United States until the drug has received FDA approval. The steps required before a drug may be marketed in the United States generally include the following:

- completion of extensive pre-clinical laboratory tests, animal studies, and formulation studies in accordance with the FDA s GLP regulations;
- submission to the FDA of an investigational new drug application, or IND, for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated at that site;
- performance of adequate and well-controlled human clinical trials in accordance with GCP requirements to establish the safety and efficacy of the drug for each proposed indication;
- submission to the FDA of an NDA after completion of all pivotal clinical trials;
- satisfactory completion of an FDA advisory committee review, if applicable
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the active pharmaceutical ingredient, or API, and finished drug product are produced and tested to assess compliance with cGMPs; and
- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States.

Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease.

Pre-clinical tests include laboratory evaluation of product chemistry, formulation and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the pre-clinical tests must comply with federal regulations and requirements, including GLP. An IND sponsor must submit the results of pre-clinical testing to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls and a proposed clinical trial protocol. Long term pre-clinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin if all other requirements, including IRB review and approval, have been met.. If the FDA raises concerns or questions about the conduct of the trial, such as whether human research subjects will be

exposed to an unreasonable health risk, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed.

Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted in compliance with federal regulations, including GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The study protocol and informed consent information for patients in clinical trials must also be submitted to an IRB, for approval at each site at which the

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clinical trial will be conducted. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB s requirements, or may impose other conditions. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their *www.clinicaltrials.gov* website.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the drug into healthy human subjects or patients, the drug is tested to assess pharmacological actions, side effects associated with increasing doses and, if possible, early evidence of effectiveness. Phase 2 usually involves trials in a limited patient population to study metabolism of the drug, pharmacokinetics, the effectiveness of the drug for a particular indication, dosage tolerance and optimum dosage, and to identify common adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 clinical trials, also called pivotal trials, are undertaken to obtain the additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit the FDA to evaluate the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug. In most cases the FDA requires two adequate and well controlled Phase 3 clinical trials to demonstrate the efficacy of the drug. A single Phase 3 clinical trial with other confirmatory evidence may be sufficient in rare instances where the study is a large multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible.

After completion of the required clinical testing, an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the United States. The NDA must include the results of all pre-clinical, clinical and other testing and a compilation of data relating to the product s pharmacology, chemistry, manufacture and controls. The cost of preparing and submitting an NDA is substantial. The submission of most NDAs is additionally subject to a substantial application user fee, and the manufacturer and/or sponsor under an approved NDA are also subject to annual product and establishment user fees. These fees are typically increased annually. Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the date of filing of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a filing decision.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency s threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product s continued safety, quality and purity.

The FDA may also refer applications for novel drug products, or drug products that present difficult questions of safety or efficacy, to an advisory committee typically a panel that includes clinicians and other experts for review, evaluation and a 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 NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCPs. Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. The FDA will not approve the product

unless compliance with cGMPs is satisfactory and the NDA contains data that provide substantial evidence that the drug is safe and effective in the indication studied.

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After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, or information, in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA s satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug s safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a Risk Evaluation and Mitigation Strategy, or REMS, to ensure that the benefits of the drug outweigh the potential risks. A REMS can include a medication guide, a communication plan for healthcare professionals and elements to assure safe use, such as special training and certification requirements for individuals who prescribe or dispense the drug, requirements that patients enroll in a registry and other measures that the FDA deems necessary to assure the safe use of the drug. The requirement for a REMS can materially affect the potential market and profitability of the drug. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs. Such supplements are typically reviewed within 10 months of receipt.

Expedited Development and Review Programs

The FDA has a Fast Track program that is intended to expedite or facilitate the process for development and review of new drug products that meet certain criteria. Specifically, new drug products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug may request that the FDA designate the drug as a Fast Track product at any time during the clinical development of the product. For a Fast Track-designated product, the FDA may consider for review sections of the marketing application on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

Any product submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug product designated for priority review in an effort to facilitate the review. Additionally, a product may be eligible for accelerated approval. Drug products studied for their safety and effectiveness in treating

serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may be eligible for accelerated approval, which means that they may

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be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or 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. As a condition of approval, the FDA may require that a sponsor of a drug product subject to accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

In addition, under the provisions of FDASIA, the FDA established the Breakthrough Therapy Designation which is intended to expedite the development and review of products that treat serious or life-threatening diseases or conditions. A breakthrough therapy is defined as a drug that 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. The designation includes all of the features of Fast Track designation, as well as more intensive FDA interaction and guidance. The Breakthrough Therapy Designation is distinct from both accelerated approval and priority review, but these can also be granted to the same product candidate if the relevant criteria are met. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy. Requests for breakthrough therapy designation will be reviewed within 60 days of receipt, and FDA will either grant or deny the request.

Fast Track designation, priority review, accelerated approval and breakthrough therapy designation do not change the standards for approval but may expedite the development or approval process by allowing for approval based on a surrogate endpoint likely to predict clinical benefit of the underlying drug, rather than through a direct measure of clinical benefit. Even if Miragen receives one of these designations for its product candidates, the FDA may later decide that its product candidates no longer meet the conditions for qualification. In addition, these designations may not provide Miragen with a material commercial advantage.

Post-Approval Requirements

Once an NDA is approved, a product may be subject to certain post-approval requirements. For instance, 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 and social media. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling.

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA. The FDA also may require post-marketing testing, known as Phase 4 testing, REMS, surveillance to monitor the effects of an approved product, or restrictions on the distribution or use of the product. In addition, quality-control, drug manufacture, packaging and labeling procedures must continue to conform to cGMPs after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies. Registration with the FDA subjects entities to periodic unannounced inspections by the FDA, during which the agency inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality-control to maintain compliance with cGMPs. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information, imposition of post-market studies or

clinical trials to assess new safety risks or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;

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fines, warning letters or holds on post-approval clinical trials;

refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product approvals;

product seizure or detention, or refusal to permit the import or export of products; or injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Foreign Regulation

In order to market any product outside of the United States, Miragen would need to comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of Miragen s products. Whether or not Miragen obtains FDA approval for a product, Miragen would need to obtain the necessary approvals by the comparable foreign regulatory authorities before Miragen can commence clinical trials or marketing of the product in foreign countries and jurisdictions.

Some countries outside of the United States have a similar process that requires the submission of a clinical trial application, or CTA, much like the IND prior to the commencement of human clinical trials. In Europe, for example, a CTA must be submitted to each country s national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country s requirements, a clinical trial may proceed in that country. To obtain regulatory approval to commercialize a new drug under European Union regulatory systems, Miragen must submit a marketing authorization application, or MAA. The MAA is similar to the NDA, with the exception of, among other things, country-specific document requirements.

In Canada, biopharmaceutical product candidates are regulated by the Food and Drugs Act and the rules and regulations promulgated thereunder, which are enforced by the Therapeutic Products Directorate of Health Canada, or TPD. Before commencing clinical trials in Canada, an applicant must complete pre-clinical studies and file a CTA with the TPD. After filing a CTA, the applicant must receive different clearance authorizations to proceed with Phase 1 clinical trials, which can then lead to Phase 2 and Phase 3 clinical trials. To obtain regulatory approval to commercialize a new drug in Canada, a new drug submission, or NDS, must be filed with the TPD. If the NDS demonstrates that the product was developed in accordance with the regulatory authorities rules, regulations and guidelines and demonstrates favorable safety and efficacy and receives a favorable risk/benefit analysis, the TPD issues a notice of compliance which allows the applicant to market the product.

Other Healthcare Laws

Although Miragen currently does not have any products on the market, Miragen s current and future business operations may be subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which Miragen conducts its 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. Some of Miragen s pre-commercial activities are subject to some of these laws.

The federal Anti-Kickback Statute makes it illegal for any person or entity, including a prescription drug manufacturer or a party acting on its behalf to knowingly and willfully, directly or indirectly, solicit, receive,

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offer, or pay any remuneration that is intended to induce the referral of business, including the purchase, order, lease of any good, facility, item or service for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. The term remuneration has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, formulary managers, and beneficiaries on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances. Several courts have interpreted the statute s intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the Anti-Kickback Statute has been violated. In addition, 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. Violations of this law are punishable by up to five years in prison, and can also result in criminal fines, civil money penalties and exclusion from participation in federal healthcare programs.

Moreover, 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 federal civil False Claims Act.

The federal civil False Claims Act prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, for payment to, or approval by, federal programs, including Medicare and Medicaid, claims for items or services, including drugs, that are false or fraudulent or not provided as claimed. Persons and entities 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, Miragen s future activities relating to the reporting of wholesaler or estimated retail prices for Miragen s products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state and third-party reimbursement for Miragen s products, and the sale and marketing of Miragen s products, are subject to scrutiny under this law. Penalties for federal civil False Claims Act violations may include up to 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.

HIPAA 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. Like 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.

The civil monetary penalties statute imposes penalties against any person or entity that, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

Also, many states have similar fraud and abuse statutes or regulations that may be broader in scope and may apply regardless of payor, in addition to items and services reimbursed under Medicaid and other state programs. Additionally, to the extent that any of Miragen s products are sold in a foreign country, Miragen may be subject to similar foreign laws.

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HIPAA, as amended by HITECH, and their implementing regulations, including the final omnibus rule published on January 25, 2013, mandates, among other things, the adoption of uniform standards for the electronic exchange of information in common healthcare transactions, as well as standards relating to the privacy and security of individually identifiable health information, which require the adoption of administrative, physical and technical safeguards to protect such information. Among other things, HITECH makes HIPAA s security standards directly applicable to business associates, defined as independent contractors or agents of covered entities that create, receive or obtain 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 and business associates, 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, certain state laws govern the privacy and security of health information in certain circumstances, some of which are more stringent than HIPAA and many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties.

The Affordable Care Act imposed, among other things, new annual reporting requirements for covered manufacturers for certain payments and other transfers of value provided to physicians and teaching hospitals, as well as certain ownership and investment interests held by physicians and their immediate family members. Failure to submit timely, accurately and completely the required information for all payments, transfers of value and ownership or investment interests 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. Certain states also mandate implementation of compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians.

Because Miragen intends to commercialize products that could be reimbursed under a federal healthcare program and other governmental healthcare programs, Miragen intends to develop a comprehensive compliance program that establishes internal control to facilitate adherence to the rules and program requirements to which Miragen will or may become subject. Although the development and implementation of compliance programs designed to establish internal control and facilitate compliance can mitigate the risk of investigation, prosecution, and penalties assessed for violations of these laws, the risks cannot be entirely eliminated.

If Miragen s operations are found to be in violation of any of such laws or any other governmental regulations that apply to Miragen, Miragen may be subject to penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, the curtailment or restructuring of Miragen s operations, exclusion from participation in federal and state healthcare programs and individual imprisonment, any of which could adversely affect Miragen s ability to operate its business and its financial results.

Health Reform

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could affect Miragen s future results of operations. There have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs.

In particular, the Affordable Care Act has had, and is expected to continue to have, a significant impact on the healthcare industry. The Affordable Care Act was designed to expand coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, among other things, the Affordable Care Act revised the definition of average manufacturer price for calculating and reporting Medicaid drug rebates on

outpatient prescription drug prices and imposed a significant annual fee on companies that manufacture or import certain branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may require Miragen to modify Miragen s business practices with

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healthcare providers and entities, and a significant number of provisions are not yet, or have only recently become, effective.

Miragen continues to evaluate the effect that the Affordable Care Act will have on Miragen s business. In the coming years, additional legislative and regulatory changes could be made to governmental health programs that could significantly impact pharmaceutical companies and the success of its product candidate.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. In August 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 to Congress proposals in spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation s automatic reduction to several government programs. These included 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 to the statute, will stay in effect through 2025 unless additional Congressional action is taken. Additionally, in January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Moreover, the Drug Supply Chain Security Act, imposes new obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing, which will be phased in over several years beginning in 2016. Among the requirements of this legislation, manufacturers will be required to provide certain information regarding the drug product to individuals and entities to which product ownership is transferred, label drug product with a product identifier, and keep certain records regarding the drug product. The transfer of information to subsequent product owners by manufacturers will eventually be required to be done electronically. Manufacturers will also be required to verify that purchasers of the manufacturers products are appropriately licensed. Further, under this new legislation, manufacturers will have drug product investigation, quarantine, disposition, and notification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

Coverage and Reimbursement

Sales of Miragen s product candidates, once approved, will depend, in part, on the extent to which the costs of Miragen s products will be covered by third-party payors, such as government health programs, private health insurers and managed care organizations. Third-party payors generally decide which drugs they will cover and establish certain reimbursement levels for such drugs. In particular, in the U.S., private health insurers and other third-party payors often provide reimbursement for products and services based on the level at which the government (through the Medicare or Medicaid programs) provides reimbursement for such treatments. Patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use its products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of its products. Sales of Miragen s product candidates, and any future product candidates, will therefore depend substantially on the extent to which the costs of Miragen s product candidates, and any future product candidates, will be paid by third-party payors. Additionally, the market for Miragen s product candidates, and any future product candidates, will depend significantly on access to third-party payors formularies without prior authorization, step therapy, or other limitations such as approved lists of treatments for which third-party payors provide coverage and reimbursement. Additionally, coverage and reimbursement for therapeutic products can differ significantly from payor to payor. One third-party payor s decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the

medical product or service, or will provide coverage at an adequate reimbursement rate. As a result, the coverage determination process will require Miragen to provide scientific and clinical support for the use of Miragen s products to each payor separately and will be a time-consuming process.

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Third-party payors are developing increasingly sophisticated methods of controlling healthcare costs and increasingly challenging the prices charged for medical products and services. Additionally, the containment of healthcare costs has become a priority of federal and state governments and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls and transparency requirements, 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 limit Miragen s net revenue and results. If these third-party payors do not consider Miragen s products to be cost-effective compared to other therapies, they may not cover Miragen s products once approved as a benefit under their plans or, if they do, the level of reimbursement may not be sufficient to allow Miragen to sell its products on a profitable basis. Decreases in third-party reimbursement for Miragen s products once approved or a decision by a third-party payor to not cover its products could reduce or eliminate utilization of Miragen s products and have an adverse effect on its 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 Miragen s products once approved or additional pricing pressures.

Facilities

Miragen occupies 27,128 square feet of headquarters office and laboratory space in Boulder, Colorado under a lease that expires in August 2020. Miragen believes that its facilities are adequate for its current needs.

Employees

As of December 31, 2016, Miragen employed 43 full-time employees. Miragen has never had a work stoppage, and none of its employees is represented by a labor organization or under any collective bargaining arrangements. Miragen considers its employee relations to be good.

Legal Proceedings

From time to time, Miragen is involved in legal proceedings in the ordinary course of business. Miragen is currently not a party to any legal proceedings that Miragen believes would have a material adverse effect on its business, financial condition or results of operations.

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SIGNAL MANAGEMENT S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of financial condition and results of operations should be read together with the section titled Selected Historical and Unaudited Pro Forma Condensed Combined Financial Information and Data Selected Historical Financial Consolidated Data of Signal in this proxy statement/prospectus/information statement and the consolidated financial statements of Signal and accompanying notes appearing elsewhere in this proxy statement/prospectus/information statement. This discussion of Signal s financial condition and results of operations contains certain statements that are not strictly historical and are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and involve a high degree of risk and uncertainty. Actual results may differ materially from those projected in the forward-looking statements due to other risks and uncertainties that exist in Signal s operations, development efforts and business environment, including those set forth in the section titled Risk Factors Risks Related to Signal in this proxy statement/prospectus/information statement, the other risks and uncertainties described in the section titled Risk Factors in this proxy statement/prospectus/information statement and the other risks and uncertainties described elsewhere in this proxy statement/prospectus/information statement. All forward-looking statements included in this proxy statement/prospectus/information statement are based on information available to Signal as of the date hereof, and Signal assumes no obligation to update any such forward-looking statement.

Overview

Signal is a commercial stage, molecular genetic diagnostic company that is currently marketing and selling its MyPRS test to physicians treating patients suffering from MM in academic institutions in all 50 states. Signal has been operating at a net loss since inception, based upon a business plan that anticipated raising additional funds through debt or equity financing to operate beyond the second quarter of 2017. Due to current market conditions, Signal s current liquidity position and its depressed stock price, Signal came to believe it would be difficult to obtain additional equity or debt financing on acceptable terms, if at all. Therefore, Signal s board of directors began discussing and evaluating its strategic opportunities to maximize stockholder value beginning near the end of 2015, including engaging in a sale of the company or a merger transaction.

Signal has incurred net losses in each year since its inception. As of September 30, 2016, Signal had an accumulated deficit of approximately $25 million. Substantially all of its net losses have resulted from costs incurred in connection with building the infrastructure to support is laboratory services business, its research and development programs and from general and administrative costs associated with its operations.

If the Merger and the sale of intellectual property assets related to Signal s MyPRS test are not completed, Signal will reconsider its strategic alternatives and would likely dissolve and liquidate its assets. Signal would be required to pay all of its debts and contractual obligations, and to set aside certain reserves for potential future claims, and there can be no assurances as to the amount or timing of available cash remaining to distribute to stockholders after paying the Signal obligations and setting aside funds for reserves.

Signal s future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- the timing and completion of the proposed Merger with Miragen;

the timing and completion of the sale of its intellectual property assets related to its one proprietary test, MyPRS; and

the costs associated with the winding down of it laboratory services business in Little Rock, Arkansas and corporate operations in Carlsbad, California.

Signal operates in only one segment and, currently, has no operations outside of the United States.

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Sources of Revenues and Expenses

Revenues

Signal generates revenues primarily from the completion of tests processed through its CAP-accredited and CLIA certified laboratory when test results are delivered to ordering physicians. During the first nine months of 2016, Signal had three major customers, including UAMS. Revenue sourced either from or through UAMS as a percentage of net revenue during the first nine months of 2016 and 2015 were 22% and 64%, respectively. Revenue sourced either from or through the other two major customers as a percentage of net revenue during the first nine months of 2016 and 2015 were 27% and 1%, and 11% and 11%, respectively.

A significant portion of Signal s revenues consist of payments or reimbursements received from various payors, including Medicare, contracted insurance companies, directly billed customers (UAMS, pharmaceutical companies, reference laboratories and hospitals) and non-contracted insurance companies. Signal reports revenues from contracted payors and directly billed customers based on the contractual rate. Medicare reimburses MyPRS based on the local coverage determination at approximately $1,900 per test and Blue Cross Blue Shield of Arkansas reimburses MyPRS based on the contractual rate of approximately $2,000 per test. Revenues from non-contracted payors are reported based on the amount expected to be collected, which is based on the historical collection experience of each payor or payor group, as appropriate. The estimates of net revenue are subject to change based on the contractual status and payment policies of third-party payors with whom Signal deals as well as anticipated changes in the healthcare industry and related legislation. Signal regularly refines its estimates in order to make estimated revenue as accurate as possible based on its most recent collection experience with each third-party payor.

Cost of Revenue

Signal s cost of revenue consists primarily of the cost of materials and supplies, labor, and other costs associated with processing specimens including pathological review, quality control analyses, delivery charges necessary to render an individualized test result, depreciation, amortization and royalty expense. Costs associated with performing tests are recorded as the tests are processed.

Research and Development Expenses

Signal s research and development expenses primarily include personnel costs, laboratory supplies, reagents, consulting costs associated with developing and validating new testing services and sponsored research agreements with leading academic institutions for clinical trials and other studies to further validate the use of MyPRS for MM and AMG.

Selling and Marketing Expenses

Signal s selling and marketing expenses consist primarily of sales commissions and support costs, salaries and related employee benefits, travel, and marketing costs for its commercial, business development, medical affairs and managed care functions.

General and Administrative Expenses

Signal s general and administrative expenses consist primarily of personnel costs, professional service fees and other costs related to its being a publicly-traded company.

Interest Expense

Interest expense primarily reflects interest on Signal s note payable related party.

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Critical Accounting Policies and Estimates

The preparation of financial statements in conformity with U.S. GAAP requires the use of estimates and assumptions that affect the reported amounts of assets and liabilities, revenues and expenses, and related disclosures in the financial statements. Critical accounting policies are those accounting policies that may be material due to the levels of subjectivity and judgment necessary to account for highly uncertain matters or the susceptibility of such matters to change, and that have a material impact on financial condition or operating performance. While Signal bases its estimates and judgments on its experience and on various other factors that it believes to be reasonable under the circumstances, actual results may differ from these estimates under different assumptions or conditions.

Signal believes the following critical accounting policies used in the preparation of its financial statements require significant judgments and estimates:

Revenue Recognition

Accounts Receivable, Contractual Allowance and Allowance for Doubtful Accounts

Stock-Based Compensation

Accounting for Income Taxes

During the nine months ended September 30, 2016, other than as discussed below, there were no significant changes in Signal s critical accounting policies and estimates.

Revenue Recognition

Signal recognizes revenue from testing services in accordance with the Financial Accounting Standards Board Accounting Standards Codification, or FASB ASC, 605, Revenue Recognition, which requires that four basic criteria be met before revenue can be recognized: (1) persuasive evidence that an arrangement exists; (2) delivery has occurred and title and the risks and rewards of ownership have been transferred to the client or services have been rendered; (3) the price is fixed or determinable; and (4) collectability is reasonably assured.

Revenues are recorded on an accrual basis when the contractual obligations are completed as tests are processed through Signal s laboratory and test results are delivered to ordering physicians. Revenues are billed to various payors, including Medicare, contracted insurance companies, directly billed customers (UAMS, pharmaceutical companies, reference laboratories and hospitals) and non-contracted insurance companies. Revenues from Medicare, contracted insurance companies and directly billed customers are reported based on the contractual rate. The difference between the amounts billed and the contractual rates from Medicare and contracted insurance companies are recorded as contractual allowances at the same time the revenue is recognized, to arrive at reported net revenue. The contractual rate is based on established agreed upon rates between Signal and the respective payor. Directly billed customers are invoiced at the contractual rate. Revenues from non-contracted insurance companies are reported based on the amount expected to be collected, which is based on the historical collection experience of each payor or payor group, as appropriate, and anticipated effects of changes in the healthcare industry, if any. The difference between the amount billed and the amount estimated to be collected from non-contracted insurance companies is recorded as a contractual

allowance at the same time the revenue is recognized, to arrive at reported net revenue. Signal does not record revenue from individuals for billings until cash is collected; as collectability is not assured at the time services are provided, therefore there are no accounts receivable from self-payors. Gross revenues from individuals have been immaterial to date.

Signal s estimates of net revenue for non-contracted insurance companies are subject to change based on the contractual status and payment policies of the third-party payors with whom Signal deals. Signal regularly refines its estimates in order to make estimated revenue as accurate as possible based on its most recent collection experience with each third-party payor. Signal regularly reviews its historical collection experience for non-

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contracted payors and anticipated changes in the healthcare industry and adjust expected revenues for current and subsequent periods accordingly, including previously recorded revenues related to outstanding accounts receivable for such non-contracted payors.

Accounts Receivable, Contractual Allowances and Allowance for Doubtful Accounts

Signal records accounts receivable net of contractual allowances and an allowance for doubtful accounts. At September 30, 2016 and December 31, 2015, contractual allowances were $3.1 million and $2.1 million, respectively. Signal estimates an allowance for doubtful accounts based on the aging of the accounts receivable and the historical collection experience for each contracted payor. When the amounts are determined to be uncollectible, they are expensed as bad debt and subsequently charged-off against the allowance. During the third quarters of 2016 and 2015, Signal recognized $7,000 and $4,000, respectively, in bad debt expense. During first nine months of 2016 and 2015, it recognized $8,000 and $32,000, respectively, in bad debt expense. During 2015 and 2014, Signal recognized $33,000 and $177,000 in bad debt expense, respectively. At September 30, 2016 and December 31, 2015, allowances for doubtful accounts were $10,000 and $0, respectively. Uncollectability of accounts receivable for a non-contracted payor is typically a reflection of an estimate in excess of actual collections and is adjusted in the period of collection as a change in estimate resulting in an increase in contractual allowances and, therefore, a reduction in current period net revenue.

The following tables present Signal s gross accounts receivable from customers outstanding by aging category reduced by total contractual and doubtful account allowances to arrive at the net accounts receivable balances at September 30, 2016 and December 31, 2015. Other than the direct bill customers, all receivables were pending approval by third-party payors as of the date that the receivables were recorded:

	September 30, 2016				
(in thousands)	**0 - 30 Days**	**31 - 60 Days**	**61 - 90 Days**	**Over 90 Days**	**Total**
Medicare	$ 270	$ 155	$ 9	$ 31	$ 465
Contracted insurance companies	53	9	4	14	80
Direct bill	151	6		3	160
Non-contracted insurance companies	365	243	286	2,239	3,133
Accounts receivable, gross	839	413	299	2,287	3,838
Less: contractual and doubtful account allowances	(450)	(274)	(235)	(2,146)	(3,105)
Accounts receivable, net	$ 389	$ 139	$ 64	$ 141	$ 733

	December 31, 2015				
(in thousands)	**0 - 30 Days**	**31 - 60 Days**	**61 - 90 Days**	**Over 90 Days**	**Total**
Medicare	$ 116	$ 55	$ 32	$ 16	$ 219
Contracted insurance companies	13		9	16	38
Direct bill	101	12	24	14	151

Non-contracted insurance companies	336	256	215	1,244	2,051
Accounts receivable, gross	566	323	280	1,290	2,459
Less: contractual allowances	(347)	(245)	(230)	(1,243)	(2,065)
Accounts receivable, net	$ 219	$ 78	$ 50	$ 47	$ 394

The day sales outstanding, or DSO, at September 30, 2016 has increased to 78 days, compared to 53 days at December 31, 2015, attributable to the growth in net accounts receivable which was influenced by the increase in both test volume and average selling price for billings to non-contracted insurance payors. Since private non-contracted insurance payors are slower to pay, Signal expects its DSO s to increase as net revenues from these payors increase.

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Stock-Based Compensation

Signal recognizes compensation expense in an amount equal to the estimated fair value of each stock award over the estimated period of service and vesting. The estimation of the fair value of each stock-based grant or issuance involves numerous assumptions by management. The use of different values by management in connection with these assumptions could produce substantially different results.

Accounting for Income Taxes

Deferred income taxes result primarily from temporary differences between financial and tax reporting. Deferred tax assets and liabilities are determined based on the difference between the financial statement basis and tax basis of assets and liabilities using enacted tax rates. Future tax benefits are subject to a valuation allowance when management is unable to conclude that Signal s deferred tax assets will more-likely-than-not be realized from the results of operations. The estimate for the valuation allowance for deferred tax assets requires management to make significant estimates and judgments about projected future operating results. If actual results differ from these projections or if management s expectations of future results change, it may be necessary to adjust the valuation allowance.

Recently Adopted Accounting Pronouncements

In March 2016, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2016-09, which simplifies several aspects of the accounting for stock-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. The update is effective for fiscal years and the interim periods within those fiscal years beginning after December 15, 2016, with early adoption permitted. Amendments related to the timing of when excess tax benefits are recognized, minimum statutory withholding requirements and forfeitures are applied using a modified retrospective transition method by means of a cumulative-effect adjustment to equity as of the beginning of the period in which the guidance is adopted. Amendments related to the presentation of employee taxes paid on the statement of cash flows when an employer withholds shares to meet the minimum statutory withholding requirement is applied retrospectively. Amendments requiring recognition of excess tax benefits and tax deficiencies in the income statement are applied prospectively. Signal elected to early adopt this guidance effective January 1, 2016. The impact of adoption of this guidance had no effect on Signal s financial position, statements of operations or statements of cash flows.

In May 2015, the FASB issued ASU No. 2015-07 that eliminates the requirement to categorize investments within the fair value hierarchy if their fair value is measured using the net asset value per share practical expedient in the FASB s fair value measurement guidance. The amendments also limit certain disclosures to investments for which the entity has elected to measure at fair value using the net asset value per share practical expedient. The amendments were applied retrospectively by removing from the fair value hierarchy any investments for which fair value is measured using the net asset value per share practical expedient. Adoption of this guidance did not have an impact on Signal s financial position or results of operations.

Recent Accounting Pronouncements

Signal has reviewed all recently issued standards and has determined that other than as disclosed above and in Note 2 to the financial statements included herein, such standards will not have a material impact on its financial statements or do not otherwise apply to its operations.

Future Accounting Pronouncements

Section 107 of the JOBS Act provides that an emerging growth company, such as Signal, can take advantage of an extended transition period for complying with new or revised accounting standards. Thus, an emerging growth

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company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. Although to date, Signal has not yet taken advantage of this delay, it has elected to avail itself of this extended transition period for adopting new or revised accounting standards in the future. Therefore, Signal will not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. As a result of this election, the financial statements may not be comparable to companies that comply with public company effective dates. In the future, Signal may elect to opt out of the extended period for adopting new or revised accounting standards. If Signal does so, it will be required to disclose such decision, which will be irrevocable.

Results of Operations

Third Quarter of 2016 Compared to the Third Quarter of 2015

Net Revenue

Net revenue was $889,000 during the third quarter of 2016, an increase of $388,000, or 77%, compared to $501,000 during the third quarter of 2015. Net revenue and tests billed during the third quarters of 2016 and 2015 were as follows:

	Three Months Ended September 30,							
	Net Revenue (in 000s)				Tests Billed			
			Increase (Decrease)				Increase (Decrease)	
	2016	2015	$	%	2016	2015	#	%
Clinical patients at U.S. hospitals and direct billed customers	$ 821	$ 421	$ 400	95%	527	343	184	54%
Research testing services	52	75	(23)	(31)%	46	94	(48)	(51)%
Pharmaceutical services	16	5	11	220%	5	10	(5)	(50)%
Total	$ 889	$ 501	$ 388	77%	578	447	131	29%

The number of tests billed for clinical patients at U.S. hospitals and direct billed customers increased 54% during the third quarter of 2016 compared to the same period in 2015 due to an increase in new hospital customers and an increase in tests sourced from existing customers. Net revenue recognized for such tests billed increased 95% during the third quarter of 2016 when compared to the same period in 2015. The increase in net revenue was driven primarily by the increased test volume and an increase in test average selling price estimates used to calculate revenue for billings to non-contracted insurance payors based on positive collections experience with such payors. Additionally, net favorable changes in estimates of $6,000 were recorded in the third quarter of 2016, related to revenues recorded in prior years. Net revenue of $421,000 in the third quarter of 2015 was reduced by $64,000 of net unfavorable changes in estimates related to revenue recorded in 2014.

Both the net revenue recognized and number of tests reported and billed for research testing services, primarily UAMS, decreased 31% and 51% during the third quarter of 2016 compared to the third quarter of 2015 primarily due to the decrease in funds available at UAMS for such services.

In Signal s pharmaceutical services business, MyPRS is being run across multiple clinical trials in connection with the development of novel treatments for patients with multiple myeloma. Signal recognized net revenue of $16,000 for services rendered during the third quarter of 2016.

Cost of Revenue

Cost of revenue was $599,000, or 67% of net revenues, during the third quarter of 2016, an increase of $22,000, or 4%, compared to $577,000, or 115% of net revenues, during the third quarter of 2015. The increase in cost of

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revenue is primarily attributable to an increase in assigned laboratory personnel costs to fulfill the higher test volumes from clinical patients at U.S. hospitals for the third quarter of 2016 and an increase in the royalties due to UAMS for the higher test volume.

Research and Development Expenses

Research and development expenses were $226,000 during the third quarter of 2016, a decrease of $27,000, or 11%, when compared to $253,000 during the third quarter of 2015. The decrease is primarily attributable to a $132,000 decrease in the usage of labor, materials and supplies for internal research projects compared to the third quarter of 2015, offset by a $105,000 increase in sponsored research programs related to research to further validate the use of MyPRS in MM and AMG.

Selling and Marketing Expenses

Selling and marketing expenses were $373,000 during the third quarter of 2016, a decrease of $423,000, or 53%, when compared to $796,000 during the third quarter of 2015. The decrease is primarily attributed to $137,000 in recruiting and hiring costs incurred during the third quarter of 2015 related to establishing Signal s medical affairs function, a $209,000 decrease in marketing projects due to one-time projects incurred in the third quarter of 2015 and a $77,000 decrease in personnel costs due to a reduction in staff during 2016.

General and Administrative Expenses

General and administrative expenses were $1.5 million during the third quarter of 2016, a decrease of $496,000, or 25%, when compared to $2.0 million during the third quarter of 2015. The decrease was primarily attributable to a $720,000 decrease in stock-based compensation expense, $40,000 in decreased expenses related to facility and other administrative costs, offset by $242,000 in increased spending related to professional services, and $22,000 in increased personnel costs related to hiring of accounting, internal billing and IT staff.

First Nine Months of 2016 Compared to the First Nine Months of 2015

Net Revenue

Net revenue was $2.6 million during the first nine months of 2016, an increase of $702,000, or 37%, compared to $1.9 million during the first nine months of 2015. Net revenue and tests billed during the first nine months of 2016 and 2015 were as follows:

	Nine Months Ended September 30,							
	Net Revenue (in 000s)				Tests Billed			
			Increase (Decrease)				Increase (Decrease)	
	2016	2015	$	%	2016	2015	#	%
Clinical patients at U.S. hospitals and direct billed customers	$ 2,368	$ 974	$ 1,394	143%	1,492	878	614	70%
Research testing services	131	900	(769)	(85)%	144	1,106	(962)	(87)%
Pharmaceutical services	82	5	77	1,540%	17	10	7	70%

Total	$ 2,581	$ 1,879	$ 702	37%	1,653	1,994	(341)	(17)%

The number of tests billed for clinical patients at U.S. hospitals and direct billed customers increased 70% during the first nine months of 2016 compared to the same period in 2015 due to an increase in new hospital customers and an increase in tests sourced from existing customers. Net revenue recognized for such tests billed increased 143% during the first nine months of 2016 when compared to the same period in 2015. The increase in net

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revenue was driven primarily by the increased test volume and an increase in test average selling price estimates used to calculate revenue for billings to non-contracted insurance payors based on positive collections experience with such payors. Additionally, net favorable changes in estimates of $229,000 were recorded in the first nine months of 2016, related to revenues recorded in prior years. Net revenue of $974,000 in the first nine months of 2015 was reduced by $137,000 of net unfavorable changes in estimates related to revenue recorded in 2014.

Both the net revenue recognized and number of tests reported and billed for research testing services, primarily UAMS, decreased 85% and 87% during the first nine months of 2016 compared to the first nine months of 2015 primarily due to the decrease in funds available at UAMS for such services.

In Signal s pharmaceutical services business, MyPRS is being run across multiple clinical trials in connection with the development of novel treatments for patients with multiple myeloma. Signal recognized net revenue of $82,000 for services rendered during the first nine months of 2016.

Cost of Revenue

Cost of revenue was $1.9 million, or 72% of net revenues, during the first nine months of 2016, a decrease of $160,000, or 8%, compared to $2.0 million, or 107% of net revenues, during the first nine months of 2015. The decrease in cost of revenue is primarily attributable to a decrease of $46,000 of assigned laboratory personnel and $160,000 decrease in laboratory supply costs, a reflection of lower test volumes from UAMS, offset by a $46,000 increase in royalty expense, related to an increase in clinical patient-related revenues.

Research and Development Expenses

Research and development expenses were $867,000 during the first nine months of 2016, an increase of $321,000, or 59%, when compared to $546,000 during the first nine months of 2015. The increase is primarily attributable to $486,000 increase in sponsored research programs related to research to further validate the use of MyPRS in MM and AMG, offset by a $165,000 decrease in the usage of labor, materials and supplies for internal research projects compared to the first nine months of 2015.

Selling and Marketing Expenses

Selling and marketing expenses were $1.4 million during the first nine months of 2016, a decrease of $366,000, or 20% when compared to $1.8 million during the first nine months of 2015. The decrease is primarily attributed to $90,000 in recruiting and hiring costs incurred during the first nine months of 2015 related to establishing a medical affairs function, a $241,000 decrease in marketing projects due to one-time projects incurred in the first nine months of 2015 and a $35,000 decrease in personnel costs due to a reduction in staff during 2016.

General and Administrative Expenses

General and administrative expenses were $5.5 million during the first nine months of 2016, a decrease of $288,000, or 5%, when compared to $5.7 million during the same period in 2015. The decrease was primarily attributable to a $750,000 decrease in stock-based compensation expense and $42,000 in decreased expenses related to facility and other administrative costs, offset by $255,000 in increased personnel costs related to hiring of accounting, internal billing and IT staff, $174,000 in increased spending related to professional services, and $75,000 in increased fees and expenses for the board of directors.

Interest Expense

Interest expense was $69,000 during the first nine months of 2016, compared to $118,000 during the first nine months of 2015. The decrease was primarily due to interest expense recorded in the third quarter of 2015 related to the increase in the principal amount of an unsecured note payable due to a related party. The increase in the principal amount of the note was deferred and was amortized to interest expense over the initial term of the note to June 30, 2015.

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Year Ended December 31, 2015 Compared to the Year Ended December 31, 2014

Net Revenue

Net revenue was $2.5 million during 2015, a decrease of $1.8 million, or 41%, compared to $4.3 million during 2014. Net revenue and tests billed during 2015 and 2014 were as follows:

	Net Revenue (in 000s)				Tests Billed			
			Increase (Decrease)				Increase (Decrease)	
	2015	2014	$	%	2015	2014	#	%
UAMS-sourced:								
Research programs	$ 954	$ 3,114	$ (2,160)	(69)%	1,170	3,225	(2,055)	(64)%
Clinical patient revenue	412	504	(92)	(18)%	346	448	(102)	(23)%
Other US hospitals and direct billed customers	1,052	668	384	57%	921	511	410	80%
Pharmaceutical services	120	34	86	253%	59	12	47	392%
Total	$ 2,538	$ 4,320	(1,782)	(41)%	2,496	4,196	(1,700)	(41)%

The net revenue recognized and number of tests reported and billed under the UAMS research programs decreased 69% and 64% respectively, in 2015 compared to 2014 primarily due to the decrease in funds available at UAMS for such programs. Signal expects continued declining revenue from the UAMS research programs.

The number of tests reported and billed for UAMS-sourced clinical patients decreased 23% in 2015 when compared to 2014 due to the normal fluctuation in patient census. Net revenue recognized for such tests billed decreased 18% in 2015 when compared to 2014. The decrease in net revenue related to the decreased test volume, offset by $73,000 of net unfavorable prior year adjustments, booked in 2015, related to revenues recorded in the prior year.

The number of tests billed for other U.S. hospitals and direct billed customers increased 80% in 2015 when compared to 2014 due to an increase in new hospital customers, a direct result of the ongoing expansion of the commercial organization and the increased marketing efforts. Net revenue recognized for such tests increased 57% in 2015 when compared to 2014. The increase in net revenue was driven by the increased test volume offset by a reduction in test average selling price estimates used to calculate revenue for billings to non-contracted insurance payors. Additionally, a net unfavorable prior year adjustment of $120,000 was booked in 2015, relating to revenues recorded in the prior year. The reduction in current year pricing estimates for these non-contracted payors was in anticipation of the potential impact of the Affordable Care Act on utilization, coupled with a review of the historical collection trends, including non-contracted payors for whom Signal does not have collection experience. Signal expects the number of new payors to continue to increase, which may affect collection trends and, therefore, revenue estimates for billings to non-contracted insurance payors.

The net revenue recognized and number of tests reported and billed under service agreements with pharmaceutical customers increased 253% and 392%, respectively, in 2015 compared to 2014 due to the master laboratory service agreements executed with two pharmaceutical companies during 2015. Signal expects revenue from its pharmaceutical services business to grow as testing volume from these two agreements increase. Signal is pursuing additional agreements with other pharmaceutical companies as well as additional projects with its two current collaborators.

Cost of Revenue

Cost of revenue was $2.5 million or 97% of net revenues, during 2015, a decrease of $894,000, or 27%, compared to $3.4 million, or 78% of net revenues, during 2014. The decrease was attributable to (1) $526,000 in decreased personnel costs, primarily related to $200,000 in decreased stock-based compensation expense, $100,000 in one-time bonuses paid in 2014, $156,000 in labor costs allocated to research and development

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projects and $109,000 in reduced employee health insurance costs related to changing insurers, and (2) $424,000 in decreased material and supply costs due to a decrease in the total tests performed. These decreases were partially offset by a $56,000 increase in other laboratory related expenses, including depreciation expense.

Research and Development Expenses

Research and development expenses were $1.0 million during 2015, an increase of $655,000, or 189%, when compared to $347,000 during 2014. The increase is due to $470,000 in increased usage of labor, materials and supplies for research projects, $15,000 in increased consulting services and $170,000 in sponsored research programs related to research to further validate the use of MyPRS in MM and AMG.

Selling and Marketing Expenses

Selling and marketing expenses were $2.6 million during 2015, an increase of $1.8 million, or 257%, when compared to $717,000 during 2014. The increase was primarily attributed to a $1.4 million increase in personnel costs related to expanding the sales and marketing function and establishing managed care, commercial and business development functions, and $432,000 of expense for new marketing projects.

General and Administrative Expenses

General and administrative expenses were $7.7 million during 2015, an increase of $835,000, or 12%, when compared to $6.9 million during 2014. The increase was primarily attributable to $1.2 million in increased personnel costs related to hiring the chief financial and information officers, and accounting, internal billing, information technology and administrative staff, $275,000 in additional costs for an incentive plan, $638,000 of increased legal, accounting and insurance expenses related to Signal being a publicly-traded company for a full year during 2015, partially offset by $1.1 million in decreased stock-based compensation expense and $144,000 in decreased bad debt expense.

Gain on Legal Settlement

In August 2013, Signal settled a lawsuit in which it was the plaintiff for a tortuous interference claim regarding a potential acquisition, of which $100,000 was recognized as a gain on legal settlement during 2014.

Interest Expense

Interest expense was $141,000 during 2015, compared to $1.0 million during 2014. The decrease was primarily attributable to the Debt Conversion that occurred in June 2014.

Liquidity and Capital Resources

Signal had cash and cash equivalents of $5.4 million at September 30, 2016 compared to $10.8 million at December 31, 2015. At September 30, 2016, it had working capital of $3.7 million.

Signal s existing cash resources will not be sufficient to meet its operating plan for the full 12-month period after the date of this proxy statement/prospectus/information statement. Based on available resources, Signal believes it can maintain its operations into the second quarter of 2017. As a result, to continue to fund operations beyond the second quarter of 2017, Signal would need to (1) raise additional capital through the issuance of equity, debt or other securities, (2) convert existing debt into equity, (3) enter into strategic partnerships, alliances, collaborations or other similar transactions or (4) a combination thereof. Signal s financial statements do not include any adjustments that

might be necessary if it is unable to continue as a going concern.

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Due to current market conditions, Signal s current liquidity position and its depressed stock price, Signal came to believe it may be difficult to obtain additional equity or debt financing on terms acceptable, if at all, thus raising substantial doubt about its ability to continue as a going concern. On October 31, 2016, Signal, Merger Sub and Miragen entered into the Merger Agreement, pursuant to which, among other things, subject to the satisfaction or waiver of the conditions set forth in the Merger Agreement, Merger Sub will merge with and into Miragen, with Miragen becoming a wholly-owned subsidiary of Signal and the surviving corporation of the Merger. If the Merger is completed, the business of Signal will become the business of Miragen as described in this proxy statement/prospectus/information statement under the caption Miragen Business. Also on October 31, 2016, Signal announced that it had entered into a non-binding letter of intent with a large global diagnostic laboratory for the sale of intellectual property assets related to Signal s MyPRS test. Subsequently on November 29, 2016, Signal and Quest Diagnostics Investments LLC entered into the Intellectual Property Purchase Agreement. Pursuant to the Intellectual Property Purchase Agreement, upon closing of the sale of the MyPRS asset transaction, Signal will receive $825,000 in cash from Quest, plus an additional $100,000 if Quest exercises the option to require Signal to operate the lab after December 31, 2016 (but not later than January 14, 2017).

Signal has no material commitments for capital expenditures at this time.

Operating activities

Cash used by operations during the first nine months of 2016 was $5.4 million, compared to $5.6 million during the first nine months of 2015.

During the first nine months of 2016, the provision of cash from changes in operating assets and liabilities of $101,000 includes a decrease in inventory of $125,000 and an increase in accounts payable and accrued liabilities of $360,000, partially offset by a $339,000 increase in accounts receivable, which primarily reflects an increase in Signal s net revenue during the first nine months of 2016 when compared to the fourth quarter of 2015, and an increase in prepaid expenses and other current assets of $45,000.

During the first nine months of 2015, the provision of cash from changes in operating assets and liabilities of $244,000 includes a $541,000 decrease in accounts receivable and a $307,000 increase in accounts payable and accrued liabilities, primarily due to higher accrued compensation, partially offset by an increase in inventory of $185,000, an increase in prepaid expenses and other current assets of $171,000 and a reduction in Signal s lease termination/abandonment payable of $248,000.

Investing activities

Net cash used by investing activities during the first nine months of 2016 and 2015 of $3,000 and $72,000, respectively, were for the purchase of property and equipment.

Financing activities

Net cash used by financing activities during the first nine months of 2016 of $124,000 consisted of $61,000 used to repurchase shares from employees to satisfy tax withholding obligations for restricted stock awards and $63,000 for repayment of Signal s capital lease obligation.

Net cash provided by financing activities during the first nine months of 2015 of $12.7 million consisted primarily of the net proceeds from Signal s public offerings of common stock in February and September 2015 of $13.1 million, partially offset by $363,000 used to repurchase shares from employees to satisfy tax withholding obligations for

restricted stock awards and $56,000 for repayment of Signal s capital lease obligation.

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Related Party Transactions

During 2014, Signal s then majority member, and current Chairman of the board of directors, through various entities controlled by such member, loaned a net amount of $795,000 to Signal to support its operations. The secured note bore interest at 8% compounded quarterly, was due on demand and collateralized by substantially all of Signal s assets. Pursuant to the terms of an exchange agreement, and prior to the corporate conversion, $27.3 million of the secured note payable as of June 17, 2014 was exchanged for 2,732,629 Class C units of Signal Genetics LLC and recorded to members equity. The remaining $1.0 million as of that date, along with an additional $45,000, which was advanced to pay for certain offering expenses, was reclassified as unsecured amounts due to related party in the consolidated balance sheet. The aggregate amount was non-interest bearing and was due on demand.

On March 6, 2015, the amounts due to related party, aggregating $1,045,000, were converted into an unsecured note payable related party, bearing interest at 8% per annum and due on demand. The principal amount of the note was increased by $60,000 over the amounts due to related party to $1,105,009 to provide the equivalent of 8% per annum interest for the period of time the amounts due to related party were held as a payable in exchange for a provision that the related party would not call the note prior to June 30, 2015. The increase in the principal amount of the note was deferred and amortized to interest expense over the initial term of the note to June 30, 2015. Interest expense related to this note during the year ended December 31, 2015 was $132,000. The note balance at December 31, 2015 was $1,105,009 and accrued interest payable of $73,000 is included in accrued liabilities in the consolidated balance sheet at December 31, 2015.

On October 31, 2016, Signal entered into the Note Amendment, modifying the principal amount of the note to $1,045,000, the original amount advanced to Signal as of June 17, 2014, and the interest of the original note to a rate per annum of 11% commencing on June 17, 2014, with interest computed on the basis of the actual number of days in a 360-day year, or Outstanding Balance. The Note Amendment also allows for the conversion of the Outstanding Balance subject to an additional 11% premium on the Outstanding Balance into shares of common stock immediately prior to the effective time of the Merger with Miragen at a conversion price equal to $5.39 per share, which was the closing price of Signal s common stock on The NASDAQ Capital Market as of the effective date of the Note Amendment. This conversion provision of the Note Amendment is subject to, among other things, approval by Signal stockholders. If the conversion of the Note Amendment is not approved by the stockholders or if the Merger Agreement is terminated prior to the completion of the Merger, the Note Amendment will not be converted into Signal s common stock and will remain outstanding.

Commitments and Contingencies

At September 30, 2016 and December 31, 2015, other than Signal s office and laboratory leases, a license agreement with UAMS and a services agreement with a third party to assist with collections from customers, it had no material commitments other than the liabilities reflected in the financial statements.

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MIRAGEN MANAGEMENT S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of financial condition and results of operations should be read together with the section titled Selected Historical and Unaudited Pro Forma Condensed Combined Financial Information and Data Selected Historical Financial Consolidated Data of Miragen in this proxy statement/prospectus/information statement and the consolidated financial statements of Miragen and accompanying notes appearing elsewhere in this proxy statement/prospectus/information statement. This discussion of Miragen s financial condition and results of operations contains certain statements that are not strictly historical and are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and involve a high degree of risk and uncertainty. Actual results may differ materially from those projected in the forward-looking statements due to other risks and uncertainties that exist in Miragen s operations, development efforts and business environment, including those set forth in the section titled Risk Factors Risks Related to Miragen in this proxy statement/prospectus/information statement, the other risks and uncertainties described in the section titled Risk Factors in this proxy statement/prospectus/information statement and the other risks and uncertainties described elsewhere in this proxy statement/prospectus/information statement. All forward-looking statements included in this proxy statement/prospectus/information statement are based on information available to Miragen as of the date hereof, and Miragen assumes no obligation to update any such forward-looking statement.

Overview

Miragen is 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. Miragen believes its 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. Miragen uses its expertise in systems biology and oligonucleotide chemistry to discover and develop a pipeline of product candidates. Miragen s two lead product candidates, MRG-106 and MRG-201, are currently in Phase 1 clinical trials. Miragen s 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. Miragen s 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 Miragen s clinical programs, it is developing a pipeline of pre-clinical product candidates. The goal of Miragen s 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) and safety of the product candidate in pre-clinical studies.

Liquidity

Miragen has no products approved for commercial sale and has not generated any revenue from product sales. From inception to September 30, 2016, Miragen has raised net cash proceeds of approximately $72 million, primarily from private placements of convertible preferred stock and bridge financings and $33.8 million in proceeds under Miragen s strategic alliance with Servier.

Miragen has never been profitable and have incurred operating losses in each year since inception. Miragen s net losses were $11.3 million for the nine months ended September 30, 2016, and $15.7 million and $5.9 million for the years ended December 31, 2015 and 2014, respectively. As of September 30, 2016, Miragen had an accumulated deficit of $61.1 million. Substantially all of Miragen s operating losses resulted from expenses

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incurred in connection with its research and development programs and from general and administrative costs associated with its operations.

Miragen expects to incur significant expenses and increasing operating losses for at least the next several years as Miragen initiates and continues the clinical development of, and seek regulatory approval for, Miragen s product candidates and add personnel necessary to operate as a public company with an advanced clinical candidate pipeline of product candidates. In addition, operating as a publicly-traded company would involve the hiring of additional financial and other personnel, upgrading financial information systems, and incurring costs associated with operating as a public company. Miragen expects that its operating losses will fluctuate significantly from quarter to quarter and year to year due to timing of clinical development programs and efforts to achieve regulatory approval.

As of September 30, 2016, Miragen had cash, cash equivalents, and short-term investments of $25.6 million. Miragen s current capital resources are sufficient to fund its planned operations for the next 12-months with or without completion of the Merger and/or the concurrent financing contemplated by the Merger Agreement. Miragen will continue to require substantial additional capital to continue its clinical development activities. Accordingly, Miragen will need to raise substantial additional capital to continue to fund its operations. The amount and timing of Miragen s future funding requirements will depend on many factors, including the pace and results of its clinical development efforts. Failure to raise capital as and when needed, on favorable terms or at all, would have a negative impact on Miragen s financial condition and its ability to develop its product candidates.

Recent Events

On October 31, 2016, Miragen entered into the Merger Agreement pursuant to which, among other things, subject to the satisfaction or waiver of the conditions set forth in the Merger Agreement, a wholly-owned subsidiary of Signal will merge with and into Miragen, with Miragen becoming a wholly-owned subsidiary of Signal and the surviving corporation of the Merger. At the closing of the Merger, each outstanding share of Miragen common stock will be converted into the right to receive approximately 0.6995 shares of common stock of Signal, without giving effect to the reverse stock split, or between 0.6995 and 0.0466 shares of common stock of Signal after giving effect to the reverse stock split, as well as the payment of cash in lieu of fractional shares. Immediately after the Merger, Miragen securityholders will own approximately 96% of the fully-diluted common stock of the combined company, with Signal securityholders owning approximately 4% of the fully-diluted common stock of the combined company, each assuming that Miragen closes its concurrent financing immediately prior to the effective time of the Merger. If the concurrent financing does not close, then Miragen s securityholders would own approximately 94% of the fully-diluted common stock of the combined company and Signal s securityholders would own approximately 6% of the fully-diluted common stock of the combined company. These estimates are based on the anticipated pre-split Exchange Ratio and post-split Exchange Ratios and are subject to adjustment.

Prior to entering into the Merger Agreement, certain third parties, including some of Miragen s existing stockholders, entered into the Subscription Agreement pursuant to which such parties have agreed, subject to the terms and conditions of such agreements, to purchase, prior to consummation of the Merger, shares of its capital stock upon the Merger for an aggregate purchase price of approximately $40.7 million. The consummation of the transactions contemplated by such agreements is conditioned upon the satisfaction or waiver of the conditions set forth in the Merger Agreement.

Revenue

Miragen s revenue primarily consists of upfront payments for licenses, and payments for other research services under the Servier Collaboration Agreement with Servier, as well as grants that Miragen has been directly and indirectly

awarded.

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In the future, Miragen may generate revenue from a combination of license fees and other upfront payments, payments for research and development services, milestone payments, product sales and royalties in connection with Miragen s current and/or future strategic alliances. Miragen expects that any revenue it generates will fluctuate from quarter-to-quarter as a result of the timing of its achievement of pre-clinical, clinical, regulatory and commercialization milestones, if at all, the timing and amount of payments relating to such milestones and the extent to which any of Miragen s products are approved and successfully commercialized by Miragen or Servier. If Servier does not elect or otherwise agree to fund its development costs pursuant to the Servier Collaboration Agreement, or Miragen or Servier fails to develop product candidates in a timely manner or obtain regulatory approval for them, Miragen s ability to generate future revenues, and its results of operations and financial position would be adversely affected.

Research and Development Expenses

Research and development expenses consist of costs associated with Miragen s research activities, including its product discovery efforts, and the development of its product candidates. Miragen s research and development expenses include:

- employee-related expenses, including salaries, benefits, and stock-based compensation;
- external research and development expenses incurred under arrangements with third parties, such as CROs, contract manufacturing organizations, consultants, and Miragen s scientific advisors;
- license fees; and
- facilities, information technology, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation of leasehold improvements and equipment, and laboratory and other supplies.

Miragen expenses research and development costs as incurred. Miragen accounts for nonrefundable advance payments for goods and services that will be used in future research and development activities as expenses when the service has been performed or when the goods have been received.

At any time, Miragen is working on multiple programs, primarily within Miragen s therapeutic areas of focus. Miragen s 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, Miragen does not generate meaningful information regarding the costs incurred for these early stage research and drug discovery programs on a specific project basis. However, Miragen is currently spending the vast majority of its research and development resources on its two lead development programs.

Since Miragen s inception in July 2007, Miragen has grown to 32 research and development personnel and has spent a total of approximately $66 million in research and development expenses through September 30, 2016.

Miragen expects its research and development expenses to increase for the foreseeable future as the company continues to conduct its ongoing clinical trials, initiates new clinical trials and advances its pre-clinical research

programs toward the clinic, including registration-enabling activities. The process of conducting clinical trials and pre-clinical studies necessary to obtain regulatory approval is costly and time consuming. Miragen, or Servier, may never succeed in achieving marketing approval for any of Miragen s product candidates.

The development of each product candidate (commencing with registration enabling toxicology studies) under the Servier Collaboration Agreement is performed pursuant to a mutually agreed upon development plan to be conducted by the parties as necessary to generate data useful for both parties to obtain regulatory approval of such product candidates. Servier is responsible for a specified percentage of the cost of research and development activities through the completion of one or more Phase 2 clinical trials and will reimburse Miragen for a specified portion of such costs Miragen incurs. The costs of Phase 3 clinical trials for each product candidate will be

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allocated between the parties at a specied percentage of costs between the parties upon the occurrence of specified events under the Servier Colloboration Agreement, including if Miragen enters into a third-party agreement for the development and/or commercialization of a product in the United States at least 180 days before the initiation of the first Phase 3 clinical trial or if Miragen subsequently enters into a U.S. partner agreement or if Miragen does not enter into a U.S. partner agreement, but files for approval in the United States using data from the Phase 3 clinical trial.

Successful development of future product candidates is highly uncertain and may not result in approved products. Completion dates and completion costs can vary significantly for each future product candidate and are difficult to predict. Miragen anticipates it 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 Miragen s ability to maintain or enter into new strategic alliances with respect to each program or potential product candidate, the scientific and clinical success of each future product candidate, and ongoing assessments as to each future product candidate s commercial potential. Miragen will need to raise additional capital and may seek additional strategic alliances in the future in order to advance its various programs.

General and Administrative Expenses

General and administrative expenses consist primarily of employee salaries and benefits, including stock-based compensation, related to Miragen s executive, finance, accounting, legal, business development, and support functions. Other general and administrative expenses include allocated facility and information technology related costs not otherwise included in research and development expenses and professional fees for auditing, tax, and legal services. Miragen expects that general and administrative expenses will increase in the future as Miragen expands its operating activities.

If Miragen completes the Merger, Miragen would become a publicly-traded company and would expect to incur significant additional costs associated with being a publicly-traded company. These increases will likely include legal fees, costs associated with Sarbanes-Oxley compliance, accounting fees, and directors and officers liability insurance premiums.

Other income (expense), net

Other income (expense) consists primarily of interest income and expense, and various income or expense items of a non-recurring nature. Miragen earns interest income from interest-bearing accounts and money market funds for cash and cash equivalents and short-term investments. Interest expense has historically been comprised of interest incurred under outstanding notes payable with Silicon Valley Bank, as well as interest and other related non-cash charges under convertible notes payable with Miragen s investors.

Critical Accounting Polices and Estimates

This management discussion and analysis of financial condition and results of operations is based on Miragen s consolidated financial statements, which have been prepared in accordance with U.S. GAAP. The preparation of these financial statements requires Miragen to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses. On an ongoing basis, Miragen evaluates these estimates and judgments. Miragen bases its estimates on historical experience and on various assumptions that Miragen believes to be reasonable under the circumstances. These estimates and assumptions form the basis for making judgments about the carrying values of assets and liabilities and the recording of expenses that are not readily apparent from other sources. Actual results may differ materially from these estimates. Miragen believes that the accounting policies discussed below are critical to understanding Miragen s historical and future performance, as these policies relate to the more significant areas

involving its judgments and estimates.

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Revenue Recognition

Miragen recognizes revenue from upfront payments for licenses or options to obtain licenses in the future, milestone payments that are generated from defined research or development events, as well as amounts for other research and development services under strategic alliance and collaboration agreements. Miragen recognizes revenue when all four of the following criteria are met: (i) persuasive evidence of an arrangement exists; (ii) products have been delivered or services rendered; (iii) the selling price is fixed or determinable; and (iv) collectability is reasonably assured.

Multiple element arrangements are examined to determine whether the deliverables can be separated or must be accounted for as a single unit of accounting. Miragen s collaboration agreement with Servier, for example, includes a combination of upfront license fees, payments for research and development activities, and milestone payments that are evaluated to determine whether each deliverable under the agreement has value to the customer on a stand-alone basis and whether reliable evidence of fair value for the deliverable exists. Deliverables in an arrangement that do not meet these separation criteria are treated as a single unit of accounting, generally applying applicable revenue recognition guidance for the final deliverable to the combined unit of accounting.

Miragen recognizes revenue from nonrefundable upfront license fees over the term of performance under the collaboration agreement. When the performance period is not specified, Miragen estimates the performance period based upon provisions contained within the agreement, such as the duration of the research or development term, the existence, or likelihood of achievement of development commitments and any other significant commitments. These advance payments are deferred and recorded as deferred revenue upon receipt, pending recognition, and are classified as a short-term or long-term liability in the accompanying consolidated balance sheets. Expected performance periods are reviewed periodically and, if applicable, the amortization period is adjusted which, Miragen may accelerate or decelerate revenue recognition. The timing of revenue recognition, specifically as it relates to the amortization of upfront license fees, is significantly influenced by Miragen s estimates.

Stock-Based Compensation

Miragen accounts for stock-based compensation expense related to stock options granted to employees and members of Miragen s board of directors under the Miragen 2008 Plan by estimating the fair value of each stock option or award on the date of grant using the Black-Scholes model. Miragen recognizes stock-based compensation expense on a straight-line basis over the vesting term.

Miragen accounts for stock options issued to non-employees by valuing the award using an option pricing model and remeasuring such awards to the current fair value until the awards are vested or a performance commitment has otherwise been reached.

Research and Development

Research and development costs are expensed as incurred and include compensation and related benefits, stock-based compensation, license fees, laboratory supplies, facilities, and overhead costs. Miragen often makes nonrefundable advance payments for goods and services that will be used in future research and development activities. These payments are capitalized and recorded as expense in the period that Miragen receives the goods or when the services are performed.

Miragen records upfront and milestone payments to acquire contractual rights to licensed technology as research and development expenses when incurred if there is uncertainty in Miragen receiving future economic benefit from the

acquired contractual rights. Miragen considers future economic benefits from acquired contractual rights to licensed technology to be uncertain until such a drug candidate is approved by the FDA or when other significant risk factors are abated.

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Clinical Trial and Pre-Clinical Study Accruals

Miragen makes estimates of its accrued expenses as of each balance sheet date in Miragen s consolidated financial statements based on certain facts and circumstances at that time. Miragen s accrued expenses for pre-clinical studies and clinical trials are based on estimates of costs incurred for services provided by CROs, manufacturing organizations, and for other trial related activities. Payments under Miragen s agreements with external service providers depend on a number of factors such as site initiation, patient screening, enrollment, delivery of reports, and other events. In accruing for these activities, Miragen obtains information from various sources and estimates level of effort or expense allocated to each period. Adjustments to Miragen s research and development expenses may be necessary in future periods as its estimates change. As these activities are generally material to Miragen s overall financial statements, subsequent changes in estimates may result in a material change in its accruals.

Results of Operations

Comparison of the nine months ended September 30, 2016 and 2015

The following table summarizes Miragen s results of operations for the nine months ended September 30, 2016 and 2015 (in thousands):

	Nine Months Ended September 30,	
	2016	**2015**
Revenue	$ 2,969	$ 4,016
Research and development expenses	9,786	9,918
General and administrative expenses	4,255	2,902
Other income (expense), net	(229)	(1,599)
Net loss	11,301	10,403

Revenue

Revenue was $3.0 million for the nine months ended September 30, 2016 compared to $4.0 million for the nine months ended September 30, 2015, which was derived primarily from the Servier Collaboration Agreement. Revenue recognized under the Servier Collaboration Agreement during the nine months ended September 30, 2016 decreased by $1.5 million as compared to the same period in 2015. This decrease is primarily the result of a decrease in funded research and development expenses of $0.9 million and a decrease in revenue recognized from prior upfront license payments Miragen received from Servier of $0.6 million. These changes were driven by planned variability in the timing and extent of research and development activities under Miragen s collaboration. In addition, Miragen recognized $0.5 million in grant revenue, which related to other research and development activities.

As of September 30, 2016, Miragen had $0.1 million of deferred revenue, which consisted of payments received from Servier under the Servier Collaboration Agreement that had not yet been recognized in accordance with Miragen s revenue recognition policies. This deferred revenue is expected to be recognized through October 2017.

Research and Development Expenses

Research and development expenses were $9.8 million during the first nine months of 2016, as compared to $9.9 million during the nine months ended September 30, 2015. This decrease of $0.1 million was driven by a $1.9 million

decrease in outsourced pre-clinical studies and manufacturing costs as Miragen completed the toxicology and manufacturing studies required to support filing two INDs in the second half of 2015. This decrease was partially offset by an increase of $0.9 million in expenses incurred during the first half of 2016 related a Phase 1 clinical trial under Miragen s MRG-201 program that began to enroll subjects during the fourth quarter for 2015

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and a Phase 1 clinical trial under Miragen s MRG-106 program that began to enroll patients in the first quarter for 2016. Miragen also incurred $0.7 million of additional wages, benefits, consulting and support expenses during the first nine months of 2016 as compared to the same period in 2015 as Miragen built out its research and development organization.

General and Administrative Expenses

General and administrative expenses were $4.3 million for the nine months ended September 30, 2016 as compared to $2.9 million for the nine months ended September 30, 2015. This increase of $1.4 million was driven in part by increased corporate legal expenses of $0.7 million that were primarily related to the Merger Agreement. Miragen s personnel costs also increased by $0.5 million in 2016 due to new employee hires and increases in compensation as compared to the prior year.

Other income (expense), net

Miragen incurred $0.2 million net other non-operating expenses during the nine months ended September 30, 2016 as compared to $1.6 million during the nine months ended September 30, 2015. This decrease was primarily related to interest expense and related charges incurred in 2015 on the $8.5 million in convertible notes payable issued to Miragen s investors in the first half of 2015, which converted into preferred stock during the fourth quarter of 2015.

Comparison of the years December 31, 2015 and 2014

The following table summarizes Miragen s results of operations for the years ended December 31, 2015 and 2014 (in thousands):

	Years Ended December 31,	
	2015	**2014**
Revenue	$ 5,004	7,641
Research and development expenses	13,312	9,488
General and administrative expenses	3,850	4,068
Other income (expense), net	(3,528)	9
Net loss	15,686	5,906

Revenue

Revenue was $5.0 million for the year ended December 31, 2015 compared to $7.6 million for the year ended December 31, 2014, which was derived solely from the Servier Collaboration Agreement for both periods. Revenue during the year ended December 31, 2015 decreased by $2.6 million as compared to prior year. This decrease is primarily the result of a decrease in revenue recognized from prior upfront license payments Miragen received from Servier as a result of a change in the amortization period due to the extension of the Servier Collaboration Agreement that occurred in May 2014. As of December 31, 2015, Miragen had $0.5 million of deferred revenue, which consisted of payments received from Servier under the Servier Collaboration Agreement that have not yet been recognized in accordance with Miragen s revenue recognition policies.

Research and Development Expenses

Research and development expenses were $13.3 million for the year ended December 31, 2015 compared to $9.5 for the year ended December 31, 2014. The change was primarily driven by an increase in Miragen s outsourced pre-clinical studies and clinical trial costs of $1.7 million for the year ended December 31, 2015, compared to the year ended December 31, 2014. This increase was due to costs incurred to complete IND enabling toxicology

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studies and for clinical trial startup activities related to the initiation of two Phase 1 clinical trials. Additionally, outsourced product manufacturing costs increased by $2.0 million for the year ended December 31, 2015, compared to the year ended December 31, 2014. This increase was due to costs incurred associated with product manufacturing for IND enabling toxicology studies and to support the initiation of two Phase 1 clinical trials.

Miragen expects its research and development expenses to increase for the foreseeable future as Miragen initiates its clinical trials in the fourth quarter, and continues to advance Miragen s pre-clinical research programs toward the clinic, including other IND enabling activities.

General and Administrative Expenses

General and administrative expenses were $3.9 million for the year ended December 31, 2015 compared to $4.1 for the year ended December 31, 2014. For the year ended December 31, 2015, personnel costs, including non-cash stock based compensation increased by $0.1 million as compared to the year ended December 31, 2014. This increase was offset by a decrease in legal expenses of $0.3 million for the year ended December 31, 2015 as compared to the year ended December 31, 2014.

Other income (expense), net

Miragen incurred $3.5 million net other non-operating expenses for the year ended December 31, 2015 compared to $9 thousand in net other non-operating income for the year ended December 31, 2014. During the year ended December 31, 2015, Miragen issued $8.5 million in convertible debt to certain investors and $5.0 million notes payable to Silicon Valley Bank. Miragen incurred interest expense of $1.6 million under its convertible notes payable, including a non-cash charge of $1.3 million for the amortization of debt discount, and $0.2 million under Miragen s notes payable. During the fourth quarter of 2015, Miragen also incurred non-cash charges of $1.7 million related to changes in the fair value of the put option and loss on extinguishment of debt when the convertible notes payable converted into preferred stock.

Under the terms of these convertible promissory notes, the notes together with accrued interest were to convert at a conversion rate equal to 75% of the per share price pad for shares of Miragen Series C convertible preferred stock. However, this provision was waived by the note holders, and in October 2015, the convertible notes and accrued interest thereon totaling $8.9 million converted into 2,003,884 shares of Miragen Series C convertible preferred stock at a conversion rate of $4.43 per share, the per share cash price paid by investors to purchase each share of Series C convertible preferred stock.

Miragen concluded that the right to receive a 25% discount on the conversion to a class of equity securities in a qualified financing was a put option that needed to be valued separately. As such, Miragen recorded proceeds from these convertible promissory notes based on the estimated fair value of the embedded put option ($2.7 million) and the convertible promissory notes, which resulted in a debt discount of $2.7 million related to the value of this put option. This debt discount was being amortized over the term of the convertible promissory notes. Upon conversion of the convertible promissory notes in October 2015, Miragen recorded a loss extinguishment of the convertible promissory notes of $1.4 million, which reflects the difference between the fair value of the shares of Series C convertible preferred stock issued upon conversion of and the value of the convertible promissory notes.

Liquidity and Capital Resources

Since Miragen s inception and through September 30, 2016, Miragen has received $72 million from the sale of its equity and convertible debt securities, $33.8 million from, primarily, upfront payments and research funding under the

Servier Collaboration Agreement and $5.0 million from outstanding notes payable to Silicon Valley Bank. As of September 30, 2016, Miragen had $5.0 million available under Miragen s loan agreement with Silicon Valley Bank. This amount is available to Miragen through July 31, 2017.

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As of September 30, 2016, Miragen had $24.6 million in cash and cash equivalents. The following table shows a summary of Miragen s cash flows for the years ended December 31, 2015 and 2014 and for the nine months ended September 30, 2016 and 2015 (in thousands):

	Year Ended December 31,		Nine Months Ended September 30,	
	2015	2014	2016	2015
Net cash (used in) provided by:				
Operating activities	$ (12,950)	$ (7,704)	$ (11,469)	$ (10,112)
Investing activities	(312)	1,901	(1,249)	(52)
Financing activities	29,383	6,995	16,081	13,419
Net increase in cash and cash equivalents	$ 16,121	$ 1,192	$ 3,363	$ 3,255

Operating Activities

Cash used in operating activities was $11.5 million for the nine months ended September 30, 2016 as compared to $10.1 million for the nine months ended September 30, 2015. The increase of $1.4 million was the result of a $0.9 million increase in net loss and $1.2 million non-cash interest expense and other charges incurred during the nine months ended 2015 related to Miragen s convertible notes. These changes were partially offset by $0.6 million changes in working capital.

Cash used in operating activities was $13.0 million for the year ended December 31, 2015 as compared to $7.7 million for the year ended December 31, 2014. The increase of $5.3 million was the result of a $9.8 million increase in net loss for the year ended December 31, 2015, offset by changes in Miragen s operating assets and liabilities and $3.4 million in non-cash interest expense and charges incurred under to its convertible notes and notes payable incurred in 2015.

Investing Activities

Net cash used in investing activities was $1.2 million during the nine months ended September 30, 2016 as compared to $52 thousand during the nine months ended September 30, 2015. This increase was primarily the result of $1.0 million in purchases of marketable securities in 2016. Miragen did not have any marketable securities during the first nine months of 2015.

Net cash used in investing activities was $0.3 million during the year ended December 31 2015 as compared to net cash provided by investing activities of $1.9 million during the year ended December 31, 2014. This change primarily was the result of $2.0 million in sales and maturities of marketable securities net of purchases in 2014. Miragen did not have any marketable securities during 2015.

Financing Activities

Net cash provided by financing activities was $16.1 million for the nine months ended September 30, 2016 as compared to $13.4 million for the nine months ended September 30, 2015. During the nine months ended September 30, 2016, Miragen received $16.1 million from the issuance of preferred stock. During the nine months ended September 30, 2015, Miragen received $8.5 million from the issuance of convertible notes to Miragen s existing

investors and $5.0 million under a loan agreement with Silicon Valley Bank.

Net cash provided by financing activities was $29.4 million for the year ended December 31, 2015 as compared to $7.0 million during the year ended December 31, 2014. During 2015, Miragen received $16.1 million from the issuance of Series C convertible preferred stock, $8.5 million from the issuance of convertible notes to Miragen s existing investors, and $5.0 million under a loan agreement with Silicon Valley Bank. During 2014, Miragen received $7.0 million from the issuance of Series B convertible preferred stock.

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Future Capital Requirements

Miragen has not generated any revenue from product sales. Miragen does not know when, or if, it will generate any revenue from product sales. Miragen does not expect to generate any revenue from product sales unless and until Miragen obtains regulatory approval for and commercializes any of Miragen s product candidates. At the same time, Miragen expects its expenses to increase in connection with its ongoing development and manufacturing activities, particularly as Miragen continues the research, development, manufacture and clinical trials of, and seeks regulatory approval for, Miragen s product candidates. Immediately prior to the closing of the Merger, Miragen expects to receive proceeds of $40.7 million from the financing contemplated to close contemporaneously with the Merger Agreement. Upon the closing of the Merger, Miragen expects to incur additional costs associated with operating as a public company. In addition, subject to obtaining regulatory approval of any of its product candidates, Miragen anticipates that Miragen will need substantial additional funding in connection with its continuing operations.

As of September 30, 2016, Miragen had approximately $25.6 million in cash, cash equivalents, and short-term investments. Miragen expects its research and development expenses to substantially increase in connection with Miragen s ongoing activities, particularly as Miragen advances its product candidates in or towards clinical development.

Miragen s future capital requirements are difficult to forecast and will depend on many factors, including but not limited to:

- the achievement of milestones under the Servier Collaboration Agreement with Servier;
- the terms and timing of any other strategic alliance, licensing and other arrangements that Miragen may establish;
- the initiation and progress of Miragen s ongoing pre-clinical studies and clinical trials for its product candidates:
- the number of programs Miragen pursues;
- the outcome, timing and cost of regulatory approvals;
- the cost and timing of hiring new employees to support Miragen s continued growth;
- the costs involved in patent filing, prosecution, and enforcement; and
- the costs and timing of having clinical supplies of Miragen s product candidates manufactured.

Miragen believes that Miragen s cash, cash equivalents, and short-term investments are sufficient to fund its anticipated operating and capital requirements through, at a minimum, through at least September 30, 2017.

Until Miragen can generate a sufficient amount of product revenue to finance its cash requirements, Miragen expects to finance its future cash needs primarily through the issuance of additional equity, including in connection with the contemplated Merger, and potentially through borrowing and strategic alliances with partner companies. To the extent that Miragen raises additional capital through the issuance of additional equity or convertible debt securities, the ownership interest of Miragen s stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of existing stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting Miragen s ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. For instance, pursuant to the terms of Miragen s credit facility with Silicon Valley Bank, Miragen cannot, without the prior written consent of Silicon Valley Bank, dispose of its assets outside the ordinary course of business, pay any dividend or make any distribution to its stockholders, incur additional specified indebtedness, engage in a change in control of Miragen or make any material change to Miragen s business. If Miragen raises additional funds through marketing and distribution arrangements or other

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collaborations, strategic alliances or licensing arrangements with third parties, Miragen may have to relinquish valuable rights to Miragen s technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to Miragen. If Miragen is unable to raise additional funds through equity or debt financings when needed, Miragen may be required to delay, limit, reduce or terminate its product development or commercialization efforts or grant rights to develop and market product candidates to third parties that Miragen would otherwise prefer to develop and market itself.

Notes Payable

In April 2015, Miragen entered into a loan and security agreement with Silicon Valley Bank to borrow up to $10 million in two separate tranches. The first tranche of $5.0 million was funded in May 2015 and is scheduled to be repaid over a 48-month period with interest only payments during the first 18 months. The second tranche of $5.0 million is available at any time during the draw period once Miragen provides Silicon Valley Bank with evidence of Miragen s achievement of specified events, including, that Miragen has achieved mechanistic proof-of-concept for Miragen s Phase 1 clinical trial of MRG-106. Accelerated payments are due under specified circumstances. Amounts outstanding bear interest at the prime rate minus 0.25% (which was 3.25% at December 31, 2015) with a final payment fee equal to 5.50% of amounts borrowed. Borrowings are secured by a priority security interest, right, and title in all business assets, excluding Miragen s intellectual property, which is subject to a negative pledge. In December 2016, this agreement was amended to, among other items, extend the draw period from December 31, 2016 to July 31, 2017.

Leases

In December 2010, Miragen entered into a lease agreement for office and lab space, or the Crestview Lease, and in 2015, Miragen amended this lease agreement to extend its term through August 2020.

In April 2013, Miragen entered into separate lease agreement for additional office space, or the Westview Lease, and in 2015, Miragen amended this lease agreement to extend its term by four months through October 2015. This lease expired in 2015 and was not renewed.

Miragen s Crestview Lease is noncancelable. Minimum base lease payments, including the impact of tenant improvement allowances, under the operating lease are recognized on a straight line basis over the full term of

the lease. Rent expense for the Crestview and Westview Leases during the nine months ended September 30, 2016 and 2015 was $0.3 million and $0.2 million, respectively. Miragen is also required to pay for a portion of the operating expenses for each facility and during the nine months ended September 30, 2016 and 2015 Miragen expensed $0.3 million and $0.2 million, respectively, related to this additional rent expense.

Collaboration and License Agreements

Strategic Alliance and Collaboration with Servier

In October 2011, Miragen entered into the Servier Collaboration Agreement with Servier for the research, development, and commercialization of RNA-targeting therapeutics in cardiovascular disease, which was subsequently amended in May 2013, May 2014, May 2015, and September 2016. Under the Servier Collaboration Agreement, Miragen granted Servier an exclusive license to research, develop, and commercialize RNA-targeting therapeutics for three targets in the cardiovascular field. As of December 31, 2016, three named targets exist under the Servier Collaboration Agreement, two of which are replaceable by Servier.

Servier s rights to each of the targets are limited to therapeutics in the cardiovascular field in their territory, which is worldwide except for the United States and Japan. Miragen retains all rights for each named target in the United States and Japan and for any products or product candidates outside of the cardiovascular field.

In connection with entering into the strategic alliance with Servier, Miragen received a nonrefundable upfront payment of $8.4 million (6.0 million) in 2011 and an additional $4.0 million (3.0 million) in 2013 when

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Servier exercised their right to name a third target under the agreement. Miragen is also eligible to receive development milestone payments of 5.8 million to 13.8 million ($6.5 million to $15.5 million as of September 30, 2016) and regulatory milestone payments of 10.0 million to 40.0 million ($11.2 million to $44.8 million as of September 30, 2016) for each target. Additionally, Miragen may receive up to 175 million ($196 million as of September 30, 2016) in commercialization milestones as well as quarterly royalty payments between the low-double digits to the mid-teens (subject to reductions for patent expiration, generic competition, third-party royalty and costs of goods) on the net sales of any licensed product commercialized by Servier. Additionally, if Miragen undergoes a change of control in specified circumstances, Servier has agreed to increase this royalty by an additional percentage in the low-single digits if it seeks to use any of the acquiror s intellectual property in the development of product candidates under the Servier Collaboration Agreement. Servier is obligated to make any such royalty payment for a specified period under the Servier Collaboration Agreement.

As part of the Servier Collaboration Agreement, Miragen established a multiple-year research collaboration, under which Miragen jointly performs agreed upon research activities directed to the identification and characterization of named targets and oligonucleotides in the cardiovascular field, which Miragen refers to as the Research Collaboration. The initial three-year term of the Research Collaboration was extended by two additional years in May 2014 and again by one additional year in September 2016 through October 2017. Servier is responsible for funding all of the costs of the Research Collaboration, as defined under the Servier Collaboration Agreement.

The development of each product candidate (commencing with registration enabling toxicology studies) under the Servier Collaboration Agreement is performed pursuant to a mutually agreed upon development plan to be conducted by the parties as necessary to generate data useful for both parties to obtain regulatory approval of such product candidates. Servier is responsible for a specified percentage of the cost of research and development activities through the completion of one or more Phase 2 clinical trials and will reimburse Miragen for a specified portion of such costs Miragen incurs. The costs of Phase 3 clinical trials for each product candidate will be allocated between the parties at a specied percentage of costs between the parties upon the occurrence of specified events under the Servier Colloboration Agreement, including if Miragen enters into a third-party agreement for the development and/or commercialization of a product in the United States at least 180 days before the initiation of the first Phase 3 clinical trial or if Miragen subsequently enters into a U.S. partner agreement or if Miragen does not enter into a U.S. partner agreement, but files for approval in the United States using data from the Phase 3 clinical trial. Miragen is responsible, by itself or through a third-party manufacturer, for the manufacture and supply of all licensed oligonucleotides during the pre-clinical phase of development under the Sevier Collaboration Agreement while Servier is primarily responsible for manufacture and supply of all licensed oligonucleotides and product during the clinical phase of development under the Servier Collaboration Agreement. The parties are each responsible for the commercial supply of any licensed product to be sold in each s respective territory under the Servier Collaboration Agreement.

Under the Servier Collaboration Agreement, Miragen also granted Servier a royalty-free, non-exclusive license to develop a companion diagnostic for any therapeutic product which may be developed by Servier under the Servier Collaboration Agreement. Miragen also granted Servier an exclusive, royalty free license to commercialize such a companion diagnostic for use in connection with such therapeutic product in its territory.

The Servier Collaboration Agreement will expire as to each underlying product candidate when Servier s royalty obligations as to such product candidate have expired. Servier may also terminate the Servier Collaboration Agreement for (i) convenience upon a specified number of days prior notice to Miragen or (ii) upon determination of a safety issue relating to development under the agreement upon a specified number of days prior notice to Miragen. Either party may terminate the Servier Collaboration Agreement upon a material breach by the other party which is not cured within a specified number of days. Miragen may also terminate the agreement if Servier challenges any of the patents licensed by Miragen to Servier.

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License Agreements with the University of Texas

As of September 30, 2016, Miragen had five UT License Agreements with the University of Texas. Under each of the UT License Agreements, the University of Texas granted Miragen exclusive and nonexclusive licenses to certain patent and technology rights. The University of Texas is a minority stockholder of Miragen.

In consideration of rights granted by the University of Texas, Miragen agreed to (i) pay a nonrefundable upfront license documentation fee in the amount of $10 thousand per license, (ii) pay an annual license maintenance fee in the amount of $10 thousand per license starting one year from the date of each agreement, (iii) reimburse the University of Texas for actual costs incurred in conjunction with the filing, prosecution, enforcement, and maintenance of patent rights prior to the effective date, and (iv) bear all future costs of and manage the filing, prosecution, enforcement, and maintenance of patent rights. In 2015 and 2014, Miragen incurred upfront and maintenance fees under the UT License Agreements totaling $0.1 million, and recorded the amounts as research and development expense. All costs related to the filing, prosecution, enforcement, and maintenance of patent and technology rights are recorded as general and administrative expense when incurred.

Under the terms of the UT License Agreements, Miragen may be obligated to make the following future milestone payments for each licensed product candidate: (i) up to $0.6 million upon the initiation of defined clinical trials, (ii) $2.0 million upon regulatory approval in the United States, and (iii) $0.5 million per region upon regulatory approval in other specified regions. Additionally, if Miragen successfully commercializes any product candidate subject to the UT License Agreements, Miragen is responsible for royalty payments in the low-single digits and payments up to a percentage in the mid-teens of any sublicense income, subject to specified exceptions, based upon net sales of such licensed products. UT s right to these royalty payments will expire as to each license agreement upon the expiration of the last patent claim subject to the applicable UT License Agreement.

The license term extends on a country by country basis until the expiration of the last to expire of the licensed patents that covers such product in such country. Upon expiration of the royalty payment obligation, Miragen will have a fully paid license in such country. Miragen may also terminate each UT License Agreement for convenience upon a specified number of days prior notice to the University of Texas. The University of Texas also has the right to earlier terminate the UT License Agreements after a defined date under specified circumstances where Miragen has effectively abandoned its research and development efforts or has no sales. The UT License Agreements will terminate under customary termination provisions including Miragen s bankruptcy or insolvency, material breach, and upon mutual written consent. Miragen has expensed all charges incurred under the UT License Agreements to date, due to the uncertainty as to future economic benefit from the acquired rights.

License Agreement with Roche Innovation Center Copenhagen A/S (formerly Santaris Pharma A/S)

In June 2010, Miragen entered into the RICC License Agreement with RICC, which was subsequently amended in October 2011 and amended and restated in December 2012. In 2014, RICC was acquired by F. Hoffmann-La Roche Ltd, or Roche, and has become a wholly owned subsidiary of Roche.

Under the RICC License Agreement, Miragen received exclusive and nonexclusive licenses from RICC to use the RICC Technology for specified uses including research, development, and commercialization of pharmaceutical products using this technology worldwide. Under the RICC License Agreement, Miragen has the right to develop and commercialize the RICC Technology directed to four specified targets and the option to obtain exclusive product licenses for up to six additional targets. The acquisition of Santaris Pharma A/S by Roche was considered a change-of-control under the RICC License Agreement, and as such, certain terms and conditions of the RICC License Agreement changed, as contemplated and in accordance with the RICC License Agreement. These changes primarily

relate to milestone payments reflected in the disclosures below. As consideration for the grant of the license and option, Miragen previously paid RICC $2.3 million and issued

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RICC 856,806 shares of Miragen s Series A convertible preferred stock, which are now owned by Roche Finance Ltd, an affiliate of Roche. If Miragen exercises its option to obtain additional product licenses or to replace the target families, Miragen will be required to make additional payments to RICC.

Under the terms of the RICC License Agreement, milestone payments were previously decreased by a specified percentage as a result of the change of control by RICC referenced above. Miragen is obligated to make future milestone payments for each licensed product for up to $5.2 million. Certain of these milestones will be increased by a specified percentage if Miragen undergoes a change in control during the term of the RICC License Agreement. If Miragen grants a third party a sublicense to the RICC Technology, in lieu of the fixed milestone payments noted above, Miragen is required to remit to Roche up to a specified percentage of the upfront and milestone payments Miragen receives under its sublicense.

If Miragen successfully commercializes any product candidate subject to the RICC License Agreements, then RICC is entitled to royalty payments in the mid-single digits on the net sales of such product, provided that if such net sales are made by a sublicensee under the RICC License Agreement, RICC is entitled to royalty payments equal to the lesser of a percentage in the mid-single digits on the net sales of such product or a specified percentage of the royalties paid to Miragen by such sublicensee, subject to specified restrictions. Miragen is obligated to make any such royalty payments until the later of (i) a specified anniversary of the first commercial sale of the applicable product or (ii) the expiration of the last valid patent claim licensed by RICC under the RICC License Agreement underlying such product. Upon the occurrence of specified events, the royalty owed to RICC will be decreased by a specified percentage.

The RICC License Agreement will terminate upon the latest of the expiration of all of RICC s royalty rights, the termination of the last Miragen target or the expiration of its right to obtain a product license for a new target under the RICC License Agreement. Miragen may also terminate the RICC License Agreement for convenience upon a specified number of days prior notice to RICC, subject to specified terms and conditions. Either party may terminate the RICC License Agreement upon an uncured material breach by the other party and RICC may terminate the RICC License Agreement upon the occurrence of other specified events that are not cured within a specified number of days.

Miragen has expensed all charges incurred under the RICC License Agreement to date, due to the uncertainty as to future economic benefit from the acquired rights.

License Agreements with the t2cure GmbH

In October 2010, Miragen entered the t2cure Agreement, with t2cure, which was subsequently amended in July 2014. Under the t2cure Agreement, Miragen received a worldwide, royalty bearing, and exclusive license to specified patent and technology rights to develop and commercialize product candidates targeted at miR-92.

In consideration of rights granted by t2cure, Miragen paid a onetime upfront fee of $46 thousand and agreed to: (i) pay an annual license maintenance fee in the amount of 3 thousand ($3 thousand at September 30, 2016), and (ii) reimburse t2cure for 100% of actual costs incurred in conjunction with the filing, prosecution, enforcement, and maintenance of patent rights prior to the effective date. All costs related to the filing, prosecution, enforcement, and maintenance of patent and technology rights are recorded as general and administrative expense when incurred.

Under the terms of the t2cure Agreement, Miragen is obligated to make the following future milestone payments for each licensed product: (i) up to $0.7 million upon the initiation of certain defined clinical trials, (ii) $2.5 million upon regulatory approval in the United States and (iii) up to $1.5 million per region upon regulatory approval in the European Union or Japan. Additionally, if Miragen successfully commercializes any product candidate subject to the

t2cure Agreement, Miragen is responsible for royalty payments in the low-single digits upon net sales of licensed products and sublicense fees equal to a percentage in the low-twenties of sublicensed

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income to Miragen. Miragen is obligated to make any such royalty payment until the later of (i) the tenth anniversary of the first commercial sale of the applicable product or (ii) the expiration of the last valid claim to a patent licensed by t2cure under the t2cure Agreement covering such product. If such patent claims expire prior to the end of the ten-year term, then the royalty owed to t2cure will be decreased by a specified percentage.

The license term extends on a country by country basis until the later of: (i) the tenth anniversary of the first commercial sale of a licensed product in a country, and (ii) the expiration of the last to expire valid claim that claims such licensed product in such country. Upon expiration of the royalty payment obligation, Miragen will have a fully paid license in such country. Miragen has the right to terminate the t2cure Agreement at will, on a country-by-country basis, after 60 days written notice. Miragen has expensed all charges incurred under the t2cure Agreement to date, due to the uncertainty as to future economic benefit from the acquired rights.

License Agreement with The Brigham and Women s Hospital

In May 2016, Miragen entered into the BWH License Agreement with BWH.

Under the BWH License Agreement, BWH granted Miragen an exclusive, worldwide license, including a right to sublicense, to specified technology and patent rights of BWH. As consideration for this exclusive license, Miragen paid BWH a specified issue fee and is obligated to pay a specified annual license fee. BWH is also entitled to milestone payments of up to $2.6 million for any of Miragen s product candidates developed based on the patent rights subject to the BWH License Agreement plus a one-time sales milestone payment of $0.25 million for all product candidates developed based on the patent rights subject to the BWH License Agreement. If Miragen were to successfully commercialize any product candidate subject to the BWH License Agreement, then BWH is entitled to royalty payments in the low-single digits on the net sales of such product. BWH s right to these royalty payments will expire upon the expiration of the last patent claim subject to BWH License Agreement. BWH is also entitled to a percentage in the low-double digits of any sublicense income from such product, subject to specified exceptions. Miragen is also responsible for all costs associated with the preparation, filing, prosecution and maintenance of the patent rights subject to the BWH License Agreement.

Additionally, Miragen is obligated to use commercially reasonable efforts to develop a product under the BWH License Agreement and to meet specified diligence milestones thereunder.

The BWH License Agreement will terminate upon the expiration of all issued patents and patent applications subject to the patent rights under the agreement. Miragen may also terminate the BWH License Agreement for convenience upon a specified number of days prior notice to BWH. BWH may terminate the BWH License Agreement upon a material breach by Miragen of its payment obligations and upon the occurrence of other specified events that are not cured within a specified number of days.

Subcontract Agreement with Yale University

In October 2014, Miragen entered into the Yale Agreement with Yale which was subsequently amended in February 2016 and November 2016. Under the Yale Agreement, Miragen agreed to provide specified services regarding the development of a proprietary compound that targets microRNA-29 in the indication of idiopathic pulmonary fibrosis. Yale entered into the Yale Agreement in connection with a grant that Yale received from the National Institutes of Health, or NIH, for the development a microRNA-29 mimicry as a potential therapy for pulmonary fibrosis.

In consideration of Miragen s services under the Yale Agreement, Yale has agreed to pay Miragen up to $1.1 million. Under the terms of the Yale Agreement, Miragen retains all rights to any and all intellectual property developed solely

by Miragen in connection with the Yale Agreement. Yale has also agreed to provide Miragen with an exclusive option to negotiate in good faith for an exclusive, royalty-bearing license from Yale for any intellectual property developed by Yale or jointly by the parties under the Yale Agreement. Yale is responsible for filing, prosecuting and maintaining foreign and domestic patent applications and patents on all inventions jointly developed by the parties under the Yale Agreement.

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The Yale Agreement terminates automatically on the date that Yale delivers its final research report to the NIH under the terms of the grant underlying the Yale Agreement. Either party may also terminate the Yale Agreement upon a specified number of days notice in the event that the NIH s grant funding is reduced or terminated or upon material breach by the other party.

Off-Balance Sheet Arrangements

Miragen has not entered into any off-balance sheet arrangements and does not have any holdings in variable interest entities.

Recent Accounting Pronouncements

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers*, an updated standard on revenue recognition. ASU No. 2014-09 provides enhancements to the quality and consistency of how revenue is reported by companies while also improving comparability in the financial statements of companies reporting using International Financial Reporting Standards or U.S. GAAP. The main purpose of the new standard is for companies to recognize revenue to depict the transfer of goods or services to customers in amounts that reflect the consideration to which a company expects to be entitled in exchange for those goods or services. The new standard also will result in enhanced disclosures about revenue, provide guidance for transactions that were not previously addressed comprehensively and improve guidance for multiple-element arrangements. In July 2015, the FASB voted to approve a one-year deferral of the effective date of ASU No. 2014-09, which will be effective for Miragen in the first quarter of fiscal year 2018 and may be applied on a full retrospective or modified retrospective approach. Miragen is currently evaluating the impact of implementation and transition approach of ASU 2014 on its financial statements and related disclosures.

In March 2016, the FASB issued ASU No. 2016-08, *Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations*. The purpose of ASU No. 2016-08 is to clarify the implementation of guidance on principal versus agent considerations. For public entities, the amendments in ASU No. 2016-08 are effective for interim and annual reporting periods beginning after December 15, 2017. Miragen is currently evaluating the impact of ASU No. 2016-08 on its financial statements and related disclosures.

In August 2014, the FASB issued ASU No. 2014-15, *Presentation of Financial Statements-Going Concern*, which defines management s responsibility to assess an entity s ability to continue as a going concern, and requires related footnote disclosures if there is substantial doubt about its ability to continue as a going concern. ASU No. 2014-15 is effective for Miragen for the fiscal year ending December 31, 2016, with early adoption permitted. Miragen is currently evaluating the impact of ASU No. 2014-15 on its financial statements and related disclosures.

In November 2015, the FASB issued ASU No. 2015-17, *Balance Sheet Classification of Deferred Taxes*. ASU No. 2015-17 requires that deferred tax liabilities and assets be classified as noncurrent in a classified statement of financial position. ASU No. 2015-17 is effective for financial statements issued for fiscal years beginning after December 15, 2016, and interim periods within those fiscal years. Miragen currently does not believe the impact of adopting ASU No. 2014-15 will have a material impact on its financial statements and related disclosures.

In January 2016, the FASB issued ASU No. 2016-01, *Recognition and Measurement of Financial Assets and Financial Liabilities*. ASU No. 2016-01 requires equity investments to be measured at fair value with changes in fair value recognized in net income; simplifies the impairment assessment of equity investments without readily determinable fair values by requiring a qualitative assessment to identify impairment; eliminates the requirement for public business entities to disclose the method(s) and significant assumptions used to estimate the fair value that is

required to be disclosed for financial instruments measured at amortized cost on the balance sheet; requires public business entities to use the exit price notion when measuring the fair value of financial instruments for disclosure purposes; requires an entity to present separately in other comprehensive income the

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portion of the total change in the fair value of a liability resulting from a change in the instrument-specific credit risk when the entity has elected to measure the liability at fair value in accordance with the fair value option for financial instruments; requires separate presentation of financial assets and financial liabilities by measurement category and form of financial assets on the balance sheet or the accompanying notes to the financial statements and clarifies that an entity should evaluate the need for a valuation allowance on a deferred tax asset related to available-for-sale securities in combination with the entity s other deferred tax assets. ASU No. 2016-01 is effective for financial statements issued for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. Miragen is currently evaluating the impact of ASU No. 2016-01 on its financial statements and related disclosures.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, which supersedes FASB ASC Topic 840, Leases (Topic 840) and provides principles for the recognition, measurement, presentation and disclosure of leases for both lessees and lessors. The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease, respectively. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than twelve months regardless of classification. Leases with a term of twelve months or less will be accounted for similar to existing guidance for operating leases. The standard is effective for annual and interim periods beginning after December 15, 2018, with early adoption permitted upon issuance. Miragen is currently evaluating the impact of ASU 2016-02 on its financial statements and related disclosures.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting*. The amendment is to simplify several aspects of the accounting for stock-based payment transactions including the income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. The amendments in ASU No. 2016-09 are effective for interim and annual reporting periods beginning after December 15, 2016. Miragen is currently assessing the impact of ASU No. 2016-09 on its financial statements and related disclosures.

In April 2016, the FASB issued ASU No. 2016-10, *Revenue from Contracts with Customer*. The new guidance is an update to ASC 606 and provides clarity on: identifying performance obligations and licensing implementation. For public companies, ASU No. 2016-10 is effective for annual periods, including interim periods within those annual periods, beginning after December 15, 2016. Miragen is currently evaluating the impact of ASU No. 2016-10 on its financial statements and related disclosures.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments Credit Losses: Measurement of Credit Losses on Financial Instruments*. ASU 2016-13 requires that expected credit losses relating to financial assets measured on an amortized cost basis and available-for-sale debt securities be recorded through an allowance for credit losses. ASU 2016-13 limits the amount of credit losses to be recognized for available-for-sale debt securities to the amount by which carrying value exceeds fair value and also requires the reversal of previously recognized credit losses if fair value increases. The new standard will be effective for Miragen on January 1, 2020. Early adoption will be available on January 1, 2019. Miragen is currently evaluating the impact of ASU 2016-13 on its financial statements and related disclosures.

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MANAGEMENT FOLLOWING THE MERGER

Executive Officers and Directors

Termination of Current Executive Officers of Signal

The employment of the current executive officers of Signal is expected to be terminated immediately prior to the completion of the Merger.

Executive Officers and Directors of the Combined Company Following the Merger

Following the Merger, the combined company s directors will consist of William S. Marshall, Ph.D., Bruce L. Booth, Ph.D., John W. Creecy, Thomas E. Hughes, Ph.D., Kevin Koch, Ph.D., Kyle A. Lefkoff and Joseph Turner.

The following table lists the names and ages as of December 31, 2016 and positions of the individuals who are expected to serve as executive officers and directors of the combined company upon completion of the Merger:

Name	Age	Position(s)
Executive Officers		
William S. Marshall, Ph.D.	53	President, Chief Executive Officer and Director
Jason A. Leverone	43	Chief Financial Officer, Secretary and Treasurer
Adam S. Levy	38	Chief Business Officer
Paul D. Rubin, M.D.	63	Executive Vice President, Research and Development
Non-Employee Directors		
Bruce L. Booth, Ph.D.	42	Director
John W. Creecy	62	Director
Thomas E. Hughes, Ph.D.	57	Director
Kevin Koch, Ph.D.	56	Director
Kyle A. Lefkoff	57	Director
Joseph L. Turner	65	Director

Executive Officers

William S. Marshall, Ph.D. Dr. Marshall has served as Miragen s president and chief executive officer and as director since the company was founded in September 2007. Prior to founding Miragen, Dr. Marshall was vice president of technology and business development for bioscience at Thermo Fisher Scientific Inc., a serving science company, from April 2005 to July 2007. Dr. Marshall was one of the scientific founders of Dharmacon, Inc., a biotechnology company, which was acquired by Fisher Scientific International Inc. in April 2004, and he served as the executive vice president for research and operations and general manager of Dharmacon from August 2002 to April 2005. Prior to joining Dharmacon, Dr. Marshall served in multiple positions at Amgen, Inc., a biotechnology company, most recently as associate director of research, site head for research and head of the nucleic acid and peptide technology department. Dr. Marshall earned a B.S. in Biochemistry from the University of Wisconsin-Madison and his Ph.D. in Chemistry at the University of Colorado at Boulder.

Miragen believes that Dr. Marshall s role as Miragen s chief executive, prior board service, and extensive experience and innovations in the field of biotechnology enable him to bring a unique perspective to the board of directors. In

addition, Dr. Marshall s academic expertise and accomplishments provide the board of directors with in-depth product and field knowledge.

Jason A. Leverone. Mr. Leverone joined Miragen in November 2008 as its senior director of finance and operations and was appointed vice president, finance in March 2010. Mr. Leverone was appointed as Miragen s

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chief financial officer in February 2012. Prior to joining Miragen, Mr. Leverone was senior director of finance and controller for Replidyne, Inc., a publicly-traded biotechnology company, from November 2005 to November 2008. Prior to joining Replidyne, Mr. Leverone was the corporate controller for CreekPath System, Inc., an international software development company, from September 2002 to October 2005. He commenced his professional career with the accounting firm of Ernst and Young LLP, where he last served a senior accountant, and then Arthur Andersen LLP, where he last served as an audit manager. Mr. Leverone is a Certified Public Accountant and earned a B.S. in Business Administration from Bryant University.

Adam S. Levy. Mr. Levy has served as Miragen s chief business officer since May 2016. Prior to joining Miragen, Mr. Levy served as a senior vice president of healthcare investment banking at Wedbush Securities Inc. from September 2013 to May 2016. From May 2011 to August 2012, Mr. Levy was employed by Merrill Lynch, Pierce, Fenner & Smith, Incorporated as vice president of healthcare investment banking. Prior to joining Merrill Lynch, Mr. Levy served as vice president of healthcare investment banking at Wedbush from October 2009 through April 2011. Mr. Levy earned a B.S. in Applied Economics from Cornell University.

Paul D. Rubin, M.D. Dr. Rubin has served as Miragen s executive vice president, research and development since November 2016. Prior to joining Miragen, Dr. Rubin served as senior vice president, research and development and chief medical officer of Xoma Corporation, a publicly-traded biotechnology company, from November 2011 to November 2016, having joined Xoma in June 2011 as its vice president, clinical development and chief medical officer. Prior to joining XOMA, Dr. Rubin was the chief medical officer at Funxional Therapeutics Ltd., a pharmaceutical company from February 2011 to June 2011. He served as chief executive officer of Resolvyx Pharmaceuticals, Inc. from 2007 to 2009 and president and chief executive officer of Critical Therapeutics, Inc. from 2002 to 2007. From 1996 to 2002, Dr. Rubin served as senior vice president, development, and later as executive vice president, research and development at Sepracor Inc. From 1993 to 1996, Dr. Rubin held senior level positions at Glaxo-Wellcome Pharmaceuticals, most recently as vice president of worldwide clinical pharmacology and early clinical development. During his tenure with Abbott Laboratories from 1987 to 1993, Dr. Rubin served as vice president, immunology and endocrinology. Dr. Rubin received a B.A. from Occidental College and his M.D. from Rush Medical College. He completed his training in internal medicine at the University of Wisconsin.

Non-Employee Directors

Bruce L. Booth, Ph.D. Dr. Booth has served as a member of Miragen s board of directors since September 2007. Dr. Booth joined Atlas Venture Associates in 2005, and currently serves as partner in its life sciences group. Prior to joining Atlas Venture, from 2004 to 2005, Dr. Booth was a principal at Caxton Health Holdings L.L.C., a healthcare-focused investment firm. Prior to joining Caxton, from 1999 to 2004, Dr. Booth was an associate principal at McKinsey & Company, a global strategic management consulting firm. Dr. Booth serves on the board of Zafgen, Inc., a publicly-traded biopharmaceutical company, and several privately-held companies. Dr. Booth earned a Ph.D. in molecular immunology from Oxford University s Nuffield Department of Medicine and a B.S. in biochemistry from Pennsylvania State University.

Miragen believes Dr. Booth is qualified to serve on its board of directors due to his years of investment in the healthcare industry and his continued service leading the boards of directors of both private and public companies, which will enable him to contribute important strategic insight to the combined company s board of directors.

John W. Creecy. Mr. Creecy has served as a member of Miragen s board of directors since April 2012. Mr. Creecy has served as the chief executive officer and a director of Remeditex Ventures, LLC, a biomedical investment company, since June 2011. Prior to joining Remeditex, Mr. Creecy served as president and chief executive officer of Hunt Petroleum Corporation from February 2001 to September 2008. Prior to Hunt, Mr. Creecy served as the chief

operating officer of the Hodges Companies, Inc. from 1988 to 2000. In addition to Miragen, Mr. Creecy sits on the boards of a number of private companies. Mr. Creecy earned a B.S. in Accounting from Texas Tech University and an M.S. in Accounting from the University of North Texas.

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Miragen believes Mr. Creecy is qualified to serve on its board of directors due to his years of investment in the biomedical industry and his experience as an executive officer, which will enable him to contribute important strategic insight to the combined company s board of directors.

Thomas E. Hughes, Ph.D. Dr. Hughes has served as a member of Miragen s board of directors since September 2009. Dr. Hughes joined Zafgen, Inc., a publicly-traded biopharmaceutical company, as the chief executive officer and as a director in October 2008 and also served as its president from October 2008 until June 2014. From 1987 to 2008, Dr. Hughes held several positions at Novartis AG (formerly Sandoz Pharmaceuticals), including vice president and global head of the cardiovascular and metabolic diseases therapeutic area at the Novartis Institutes for BioMedical Research in Cambridge, MA. Dr. Hughes also serves as a member of the scientific advisory board for Navitor Therapeutics, a discovery-stage biopharmaceutical company, and as a member of the strategic advisory board for Broadview Ventures, an early-stage investment company. Dr. Hughes earned a Ph.D. in nutritional biochemistry from Tufts University, an M.S. in Zoology from Virginia Polytechnic Institute & State University and a B.A. in biology from Franklin and Marshall College.

Miragen believes Dr. Hughes is qualified to serve on its board of directors due to his years of experience in the biotechnology industry and service on both public and private boards of directors of biopharmaceutical companies, which will enable him to contribute important strategic insight to the combined company s board of directors.

Kevin Koch, Ph.D. Dr. Koch has served as a member of Miragen s board of directors since July 2016. Dr. Koch has served as a venture partner at OrbiMed Advisors, LLC since May 2016. Prior to joining OrbiMed, Dr. Koch acted as a consultant in the biotech industry from September 2015 to May 2016. Prior to acting as a consultant, Dr. Koch served as the senior vice president, drug discovery, chemical and molecular therapeutics, at Biogen, Inc. from December 2013 to September 2015. Prior to joining Dr. Koch, founded Array BioPharma Inc., a publicly-traded biopharmaceutical company, and served as its president, chief scientific officer and a member of its board of directors from May 1998 to November 2013. Prior to forming Array, Dr. Koch was an associate director of medicinal chemistry and project leader for the protease inhibitor and new technologies group for Amgen Inc. from 1995 to 1998. From 1988 until 1995, Dr. Koch held various research positions within the Central Research Division of Pfizer, Inc., including senior research investigator and senior research scientist. Dr. Koch earned a B.S. in chemistry and in biochemistry from the State University of New York at Stony Brook and a Ph.D. in synthetic organic chemistry from the University of Rochester.

Miragen believes Dr. Koch is qualified to serve on its board of directors due to his years of experience in the biotechnology industry and service on both public and private boards of biopharmaceutical companies, which will enable him to contribute important strategic insight to the combined company s board of directors.

Kyle A. Lefkoff. Mr. Lefkoff has served as a member of Miragen s board of directors since September 2007. Mr. Lefkoff has served as a general partner of Boulder Ventures, Ltd, a venture capital firm, since its founding in 1995. From 1986 until 1995, Mr. Lefkoff was employed by Colorado Venture Management, a venture capital firm, as a general partner. Mr. Lefkoff serves as chairman of the board of directors of Array BioPharma Inc., a publicly-traded biopharmaceutical company, and is a director of number of private companies. Mr. Lefkoff earned a B.A. in Economics from Vassar College, completed a fellowship in Economic History at the London School of Economics and has an M.B.A. in Finance at the University of Chicago.

Miragen believes Mr. Lefkoff is qualified to serve on its board of directors due to his years of venture capital experience and his continued service leading the boards of directors of both private and public biopharmaceutical companies, which will enable him to contribute important strategic insight to the combined company s board of directors.

Joseph L. Turner. Mr. Turner will be appointed as a member of Miragen s board of directors effective as the closing of the Merger. Mr. Turner served on the boards of directors and is the chair of the audit committees of

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Corcept Therapeutics, Inc., a publicly-traded pharmaceutical company, from 2012 to May 2016, Kythera Biopharmaceuticals, Inc., a publicly-traded pharmaceutical company, from 2008 until Kythera s acquisition by Allergan Inc. October 2015, and Sophiris Bio, a publicly-traded pharmaceutical company from 2013 to May 2016. From July 2010 until its acquisition by Grupo Ferrer Internacional, S.A. in June 2016, Mr. Turner served on the board of directors and as a chair of the audit committee of Alexza Pharmaceuticals, Inc., a publicly-traded pharmaceutical company. In 2012, Mr. Turner served on the board of directors and as chair of the audit committee of Allos Therapeutics, Inc., a publicly-traded pharmaceutical company, until its acquisition by Spectrum Pharmaceuticals Inc. in September 2012. From 2010 through 2012, he served on the board of directors and as a member of the audit committee of QLT Inc., a publicly-traded biotechnology company. In 2008, Mr. Turner served as a director and member of the audit committee of SGX Pharmaceuticals Inc., a publicly-traded pharmaceutical company. Mr. Turner served as Chief Financial Officer at Myogen, Inc., a publicly-traded biopharmaceutical company, from 1999 until it was acquired by Gilead Sciences in 2006. Previously, Mr. Turner was the chief financial officer at Centaur Pharmaceuticals, Inc. and served as Chief Financial Officer and Vice President, Finance and Administration at Cortech, Inc. Since 2009, Mr. Turner has also served on the board of managers of Swarthmore College where at various times he has served on its executive committee, finance committee, audit committee, academic affairs committee (which he currently chairs) and student affairs committee and property committee. In 2013 until 2015, Mr. Turner served on the board of directors of the Linda Crnic Institute for Down Syndrome at the University of Colorado Medical School. Mr. Turner has an M.B.A. from the University of North Carolina at Chapel Hill, an M.A. in molecular biology from the University of Colorado and a B.A. in chemistry from Swarthmore College.

Miragen believes Mr. Turner is qualified to serve on its board of directors due to his years of service on both public and private boards of directors of pharmaceutical companies, including service on audit committees and extensive finance experience, which will enable him to contribute important strategic insight to the combined company s board of directors.

Board of Directors of the Combined Company Following the Merger

Signal s board of directors currently consists of five directors consisting of Bennett S. LeBow, Samuel D. Riccitelli, David A. Gonyer, Douglas A. Schuling and Robin L. Smith, M.D. Following the Merger, none of the current Signal directors will serve as directors of the combined company and the combined company s directors will consist of seven members of Miragen s board of directors, namely William S. Marshall, Ph.D., Bruce L. Booth, Ph.D., John W. Creecy, Thomas E. Hughes, Ph.D., Kevin Koch, Ph.D., Kyle A. Lefkoff and Joseph L. Turner.

There are no family relationships among any of the current Signal directors and executive officers, and there are no family relationships among any of the proposed combined company directors and officers.

Director Independence

NASDAQ s listing standards require that Signal s board of directors consist of a majority of independent directors, as determined under the applicable rules and regulations of The NASDAQ Stock Market LLC. The board of directors has determined that each of Messrs. Gonyer and Schuling and Dr. Smith qualify as an independent director and that neither Messrs. LeBow nor Riccitelli qualify as an independent director.

Based upon information requested from and provided by each proposed director concerning his or her background, employment and affiliations, including family relationships, other than Dr. Marshall by virtue of his position as chief executive officer of Miragen, Miragen s board of directors believes that each of Drs. Booth, Hughes and Koch and Messrs. Creecy, Lefkoff and Turner will qualify as an independent director following the completion of the Merger.

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Committees of the Board of Directors

Signal s board of directors currently has, and following the completion of the Merger will continue to have, the following committees: audit committee, a compensation committee and a nominating and corporate governance committee.

Audit Committee

The responsibilities of Signal s audit committee include the following:

- appointing, approving the compensation of, and assessing the independence of Signal s registered public accounting firm;
- overseeing the work of Signal s independent registered public accounting firm, including through the receipt and consideration of reports from that firm;
- reviewing and discussing with management and Signal s independent registered public accounting firm its annual and quarterly financial statements and related disclosures;
- monitoring Signal s internal control over financial reporting, disclosure controls and procedures;
- overseeing Signal s internal audit function; and
- discussing Signal s risk management policies.

The audit committee currently consists of Mr. Gonyer, Mr. Schuling and Dr. Smith. Signal s board of directors has determined that Mr. Schuling is an audit committee financial expert as defined in Item 407(d)(5) of Regulation S-K. Mr. Schuling also serves as the chairman of Signal s audit committee

The audit committee of the combined company is expected to retain these duties and responsibilities following completion of the Merger.

Following the closing of the Merger, the members of the audit committee are expected to be Mr. Turner, who is expected to serve as chairman and as an audit committee financial expert as defined in Item 407(d)(5) of Regulation S-K, Messrs. Lefkoff and Creecy. To qualify as independent to serve on Signal s audit committee, listing standards of The NASDAQ Capital Market and the applicable rules of the SEC require that a director not accept any consulting, advisory, or other compensatory fee from Signal, other than for service as a director, or be an affiliated person of Signal. Signal s board of directors has concluded that the current composition of the audit committee meets the requirements for independence under the rules and regulations of The NASDAQ Stock Market LLC and of the SEC. Miragen believes that, following completion of the Merger, the composition of the audit committee will comply with the applicable requirements of the rules and regulations of The NASDAQ Stock Market LLC and of the SEC.

Compensation Committee

The responsibilities of Signal s compensation committee include the following:

- reviewing and approving annually the corporate goals and objectives applicable to the compensation of Signal s chief executive officer, evaluating at least annually the chief executive officer s performance in light of those goals and objectives, and determining and approving the chief executive officer s compensation level based on this evaluation

- reviewing and approving the compensation of Signal s directors and all other executive officers;

- reviewing and approving and, when appropriate, recommending to Signal s board of directors for approval, incentive compensation plans and equity-based plans, and where appropriate or required, recommending for approval by Signal stockholders, the adoption, amendment or termination of such plans; and administering such plans;

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reviewing and approving the executive compensation information included in Signal s annual report on Form 10-K and proxy statement

reviewing and approving or providing recommendations with respect to any employment agreements or severance arrangements or plans; and

reviewing director compensation and recommending any changes to the board of directors.

The current members of Signal s compensation committee are Mr. Gonyer, Mr. Schuling and Dr. Smith. Dr. Smith is the chair of Signal s compensation committee.

The compensation committee of the combined company is expected to retain these duties and responsibilities following completion of the Merger.

Following the closing of the Merger, the members of the compensation committee are expected to be Dr. Hughes, who is expected to serve as chairman, and Dr. Booth. To qualify as independent to serve on Signal s compensation committee, the listing standards of The NASDAQ Capital Market require a director not to accept any consulting, advisory, or other compensatory fee from Signal, other than for service on Signal s board of directors, and that Signal s board of directors consider whether a director is affiliated with Signal and, if so, whether such affiliation would impair the director s judgment as a member of Signal s compensation committee. Signal s board of directors has concluded that the composition of the compensation committee meets the requirements for independence under the rules and regulations of the NASDAQ Stock Market LLC and of the SEC. Miragen believes that, after the completion of the Merger, the composition of the compensation committee will meet the requirements for independence under, and the functioning of such compensation committee will comply with any applicable requirements of the rules and regulations of The NASDAQ Stock Market LLC and of the SEC.

Nominating and Corporate Governance Committee

The responsibilities of Signal s Nominating and Corporate Governance Committee include the following:

identifying and recommending candidates to fill vacancies on the board of directors and for election by the stockholders;

recommending committee and chairperson assignments for directors to the board of directors;

developing, subject to the board of directors approval, a process for an annual evaluation of the board of directors and its committees and to oversee the conduct of this annual evaluation;

overseeing Signal s corporate governance practices, including reviewing and recommending to the board of directors for approval any changes to the documents and policies in Signal s corporate governance framework, including its certificate of incorporation and bylaws; and

monitoring compliance with Signal s Code of Business Conduct and Ethics, investigating alleged breaches or violations thereof and enforcing its provisions.

Board candidates are considered by Signal s nominating and corporate governance committee on a case-by-case basis. A candidate for election to Signal s board of directors must possess the ability to apply good business judgment and must be in a position to properly exercise his or her duties of loyalty and care in his or her representation of the interests of stockholders. Candidates should also exhibit proven leadership capabilities, high integrity and experience with a high level of responsibilities within their chosen fields, and have the ability to quickly grasp complex principles of business, finance, and transactions regarding Signal s industry. In general, preferred candidates will currently hold, or have recently held, an established executive level position and have extensive experience in business, finance, law, science, research, or government. Signal s nominating and corporate governance committee will consider these criteria for nominees identified by the committee, by stockholders, or through other sources. When current members of Signal s

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board of directors are considered for nomination for reelection, Signals nominating and corporate governance committee takes into consideration their prior contributions to Signal s board of directors and performance as well as the composition of Signal s board of directors as a whole, including whether Signal s board of directors reflects the appropriate balance of independence, sound judgment, business specialization, technical skills, diversity, and other desired qualities. Signal s nominating and corporate governance committee makes a preliminary assessment of each proposed nominee based upon the résumé and biographical information, an indication of the individual s willingness to serve, and other relevant information. This information will be evaluated against the criteria set forth above and Signal s specific needs at that time. Based upon a preliminary assessment of the candidate(s), those who appear best suited to meet Signal s needs may be invited to participate in a series of interviews, which are used as a further means of evaluating potential candidates. On the basis of information learned during this process, Signal s nominating and corporate governance committee will determine which nominee(s) to submit for election. Signal s nominating and corporate governance committee uses the same process for evaluating all nominees, regardless of the original source of the nomination.

Signal s nominating and corporate governance committee and its board of directors believe that diversity along multiple dimensions, including opinions, skills, perspectives, personal and professional experiences and other differentiating characteristics, is an important element of its nomination recommendations. Signal s board of directors considers each nominee in the context of the board as a whole, with the objective of assembling a board of directors that can best maintain the success of Signal s business. Although Signal s board of directors and nominating and corporate governance committee does not have a formal diversity policy, Signal s nominating and corporate governance committee and board of directors periodically review the membership of the board of directors in light of Signal s business and strategic objectives, consider whether the directors possess the requisite skills, experience and perspectives to oversee Signal in achieving those goals, and may seek additional directors from time to time as a result of its considerations.

The current members of Signal s nominating and corporate governance committee are Mr. Gonyer, Mr. Schuling and Dr. Smith, each of whom has been determined by Signal s board of directors to be independent under the rules and regulations of The NASDAQ Stock Market LLC. Mr. Gonyer is the chair of the nominating and corporate governance committee.

Signal s nominating and corporate governance committee of the combined company is expected to retain these duties and responsibilities following completion of the Merger.

Following the closing of the Merger, the members of Signal s nominating and corporate governance committee are expected to be Dr. Koch, who is expected to serve as chairman, and Dr. Hughes.

Director Compensation

Miragen does not currently have a director compensation policy, and, except for the compensation for Drs. Hughes and Koch discussed below, none of Miragen s non-employee directors received cash compensation for service during 2016. However, Miragen does provide reimbursement for reasonable out-of-pocket expenses incurred for attending meetings of Miragen s board of directors or any committees thereof.

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The following table sets forth compensation earned and paid to each Miragen non-employee director for service as a director during 2016:

Director Compensation(1)

Name	Fees Paid in Cash	Option Awards(2)	Stock Awards	Total
Bruce L. Booth, Ph.D.	$	$	$	$
John W. Creecy				
Marvin H. Caruthers, Ph.D.(3)				
Thomas E. Hughes, Ph.D.(4)	27,000	25,736		52,736
Kyle A. Lefkoff				
Kevin Koch, Ph.D.(4)	25,000	20,397		45,397
Reza Halse, Ph.D.				

(1) The table does not include Mr. Turner, because he was not a member of Miragen s board of directors in the year ended December 31, 2016. Dr. Marshall, Miragen s president and chief executive officer, is also a director but does not receive any additional compensation for his service as a director. Dr. Marshall s compensation as an executive officer is set forth below under *Management Following the Merger Executive Compensation Summary Compensation Table*.

(2) The amounts reflect the full grant date fair value for awards granted during the year ended December 31, 2016. The grant date fair value was computed in accordance with ASC Topic 718, Compensation *Stock Compensation*.

(3) Dr. Caruthers resigned from Miragen s board of directors in July 2016.

(4) Miragen provides Drs. Hughes and Koch compensation of $25,000 on an annual basis for serving as a member of Miragen s board of directors. Additionally, Miragen pays Dr. Hughes a fee of $2,000 for each meeting of the scientific advisory board he attends as an advisor.

Each of Drs. Hughes and Koch have also been previously awarded options to purchase shares of Miragen s common stock, at an exercise price equal to the fair market value of Miragen s common stock at the time of grant. Dr. Hughes stock option awards include (i) an option to purchase 20,000 shares granted in September 2009 with an exercise price of $0.40 per share that was exercised in full in October 2016, (ii) an option to purchase 16,000 shares granted in June 2012 with an exercise price of $0.86 per share that is vested in full and (iii) an option to purchase 19,500 shares granted in February 2016 with an exercise price of $0.74 per share that vests in twelve equal installments on a quarterly basis beginning in the second quarter of 2016. Dr. Koch s stock option award includes an option to purchase 41,600 shares granted in August 2016 with an exercise price of $0.74 per share, that vests in twelve equal installments on a quarterly basis beginning in the fourth quarter of 2016.

While Miragen does not currently have a director compensation policy, in November 2016, Miragen s board of directors adopted a non-employee director cash and equity compensation policy to be effective upon the closing of the Merger. Under this policy the combined company will pay each of its non-employee directors a cash stipend for service on its board of directors and, if applicable, on the audit committee, compensation committee and nominating and corporate governance committee. Each of the combined company s non-employee directors will receive an additional stipend if they serve as the chairperson of the compensation committee, nominating and corporate governance committee or audit committee or serve as the non-executive chairperson. The stipends payable to each non-employee directors for service on the combined company s board of directors are as follows:

	Member Annual Service Stipend(1)	Chairperson Annual Service Stipend(1)(2)
Board of directors	$ 35,000	$
Audit committee	7,500	15,000
Compensation committee	5,000	10,000
Nominating and corporate governance committee	3,750	7,500
Non-Executive Chairperson	30,000	N/A

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(1) Each non-employee director has the right to elect to receive all or a portion of his or her annual cash compensation under the policy in the form of either cash, quarterly restricted common stock based on the closing price of the combined company s common stock on The NASDAQ Capital Market on the date of grant, or quarterly stock options to purchase common stock based on the Black-Scholes option-pricing model as of the date of grant. Any such election will be made before the start of the fiscal year and with any such stock options or restricted common stock elected by the directors to be vested upon grant, with stock options to expire ten years from the date of grant;
(2) Chairpersons will not receive a stipend for being a member of the applicable committee.

In addition, the cash compensation described above each member of the combined company s board of directors will receive an automatic option grant to purchase 12,000 shares (subject to adjustment for stock splits and similar matters) of the combined company s common stock at each annual meeting when such director is re-elected with an exercise price equal to the fair market value of a share of the combined company s common stock on such date. Each option grant will vest in full on the earlier of the one year anniversary of the date of grant or the combined company s next annual meeting.

Each new director elected or appointed to the combined company s board of directors will receive an initial option grant to purchase 24,000 shares (subject to adjustment for stock splits and similar matters) of the combined company s common stock upon such director s appointment or election with an exercise price equal to the fair market value of a share of the combined company s common stock on such date. Each option grant will vest in 36 equal monthly installments.

Compensation Committee Interlocks and Insider Participation

Following the completion of the Merger, the members of Signal s compensation committee are expected to be Thomas E. Hughes, Ph.D., who is expected to serve as chairman, and Bruce L. Booth, Ph.D. Each member of the Compensation Committee is expected to be an outside director as that term is defined in Section 162(m) of the Code, a non-employee director within the meaning of Rule 16b-3 of the rules promulgated under the Exchange Act and independent within the meaning of the independent director guidelines of The NASDAQ Stock Market LLC. None of the proposed combined company s executive officers serves as a member of the board of directors or compensation committee of any entity that has one or more executive officers who is proposed to serve on the combined company s board of directors or compensation committee following the completion of the Merger.

Executive Compensation

Miragen s executive officers for the year ended December 31, 2016 and who will serve as executive officers of the combined company following the Merger are referred to herein as the named executive officers. The named executive officers and their current positions are as follows:

William S. Marshall, Ph.D., President and Chief Executive Officer;

Adam S. Levy, Chief Business Officer; and

Paul D. Rubin, M.D., Executive Vice President, Research and Development.

Jason A. Leverone, Miragen s chief financial officer, will also serve as an executive officer of the combined company following the Merger.

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Summary Compensation Table

The following table provides information regarding the named executive officers of Miragen during the fiscal year ended December 31, 2016 who will serve as executive officers of the combined company. For the management of the combined company after the closing of the Merger, see *Management Following the Merger Executive Officers and Directors Executive Officers and Directors of the Combined Company Following the Merger* beginning on page 247.

Name and Principal Position	Fiscal Year	Salary	Option Awards(1)	Non-Equity Incentive Plan Compensation	All Other Compensation	Total
William S. Marshall, Ph.D.	2016	$ 340,000	$ 109,425	$ 200,056	$ 7,085(2)	$ 656,566
President and Chief Executive Officer	2015	$ 340,000	$	$ 113,101	$ 5,000(3)	$ 458,101
Adam S. Levy	2016	$ 207,885	$ 112,812	$ 150,000	$ 20,385(4)	$ 491,082
Chief Business Officer						
Paul D. Rubin, M.D.	2016	$ 124,375	$ 807,919	$ 108,575	$	$ 1,040,869
Executive Vice President, Research and Development						

(1) The amounts reflect the full grant date fair value for awards granted during 2016. The grant date fair value was computed in accordance with ASC Topic 718, Compensation *Stock Compensation*.
(2) Includes payment of disability insurance premiums for Dr. Marshall s benefit.
(3) Includes payment of life insurance premiums for Dr. Marshall s benefit.
(4) Includes payment of relocation reimbursements to Mr. Levy.

Narrative Disclosure to Summary Compensation Table

Base Salary

In 2015, Miragen s compensation committee and board of directors approved base salaries for Miragen s management team, resulting in an annual base salary of $340,000 for Dr. Marshall.

In 2016, Miragen s compensation committee and board of directors approved base salaries for Miragen s management team, resulting in an annual base salary of $340,000 for Dr. Marshall. In April 2016 and October 2016, Miragen entered into offers letter with Mr. Levy and Dr. Rubin, respectively, pursuant to which Miragen agreed to pay Mr. Levy an annual salary of $300,000 and Dr. Rubin an annual salary of $395,000.

Annual Bonuses

Miragen s board of directors and compensation committee may make special cash bonus awards in their discretion. In February 2016, Miragen s compensation committee recommended and Miragen s board of directors approved, a discretionary cash bonus to Dr. Marshall of $113,101 in recognition of his services in the year ended December 31, 2015 and in accordance with the terms of Dr. Marshall s employment agreement with the company. In January 2017,

Miragen s compensation committee awarded Mr. Levy and Dr. Rubin discretionary cash bonuses of $150,000 and $33,575, respectively, in recognition of their services provided in the year ended December 31, 2016 and in accordance with the terms of each s offer letter. The compensation committee also awarded Dr. Rubin a retention bonus of $75,000 in accordance with the terms of Dr. Rubin s offer letter. In January 2017, Miragen s compensation committee recommended and Miragen s board of directors approved, a discretionary cash bonus to Dr. Marshall of $200,056 in recognition of his services in the year ended December 31, 2016 and in accordance with the terms of Dr. Marshall s employment agreement with the company. These bonus amounts, to the extent they were in recognition for Dr. Marshall s, Mr. Levy s and Dr. Rubin s performance during the indicated year, are reflected in the Non-Equity Incentive Plan Compensation column of the Summary Compensation Table above for the indicated year.

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Stock Options

Miragen s compensation committee and the board of directors elected not to grant stock option awards to any of Miragen s named executive officers in 2015.

In February 2016, Miragen s compensation committee awarded to Dr. Marshall an option to purchase 223,000 shares of its common stock. This option has an exercise price of $0.74 per share and vests monthly over a period of four years.

In June 2016, in connection with the commencement of Mr. Levy s employment with Miragen, Miragen s board of directors approved the grant of an option to Mr. Levy to purchase 230,883 shares of its common stock. This option has an exercise price of $0.74 per share and vests as to 25% of the shares subject to the option in May 2017 with the remainder vesting monthly over a period of three years thereafter.

In November 2016, in connection with the commencement of Dr. Rubin s employment with Miragen, Miragen s board of directors approved the grant of an option to Dr. Rubin to purchase 288,604 shares of its common stock. This option has an exercise price of $4.00 per share and vests as to 25% of the shares subject to the option in November 2017 with the remainder vesting monthly over a period of three years thereafter.

Outstanding Equity Awards at Fiscal Year-End

The following table presents the outstanding equity awards held by each of Miragen s named executive officers as of December 31, 2016. Neither of the named executive officers of Miragen exercised options to purchase Miragen common stock in 2016.

Name	Number of securities underlying unexercised options exercisable	Number of securities underlying unexercised options unexercisable	Option Exercise price ($)	Option Grant Date	Option Expiration date
William S. Marshall, Ph.D.	164,726		0.40	7/31/2008	7/30/2018
	328,500		0.86	6/15/2012	6/14/2022
	46,458	176,542(1)(2)	0.74	2/22/2016	2/21/2026
Adam S. Levy		230,883(3)(4)	0.74	6/15/2016	6/14/2026
Paul D. Rubin, M.D.		288,604(3)(5)	4.00	11/30/2016	11/29/2026

(1) The remaining portion of these options to purchase common stock vest at the rate of 1/48th of the number of total shares subject to the option on a monthly basis as measured from the date of grant.

(2) If Miragen terminates Dr. Marshall s employment without cause or Dr. Marshall resigns for good reason, then this option will immediately vest the equivalent of twelve months vesting; provided, if such termination or resignation occurs within one month prior to or thirteen months following a change of control, then this option shall vest in full.

(3) If Miragen terminates Mr. Levy s or Dr. Rubin s, as applicable, employment without cause or Mr. Levy or Dr. Rubin, as applicable, resigns for good reason, then this option will immediately vest the equivalent of 12 months vesting.
(4) 25% of the shares subject to this option vest on May 16, 2017 with the remainder vesting monthly over a period of three years thereafter.
(5) 25% of the shares subject to this option vest on November 16, 2017 with the remainder vesting monthly over a period of three years thereafter.

Upon completion of the Merger, each of the above options will convert into an option to purchase common stock of Signal, with the number of shares and exercise price being appropriately adjusted to reflect the Exchange Ratio in the Merger. See *The Merger Stock Options and Warrants* beginning on page 114.

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Employment Agreements and Potential Payments Upon Termination of Employment or Change in Control

Miragen has entered into employment agreements with each of its named executive officers described below, and standard confidential information and/or inventions assignment agreements, under which each of its named executive officers has agreed not to disclose Miragen s confidential information.

William S. Marshall, Ph.D.

2008 Employment Agreement. In May 2008, Miragen entered into an employment agreement with Dr. Marshall, its president and chief executive officer. Under this employment agreement, Dr. Marshall is entitled to an annual base salary of $250,000 (subject to review and adjustment in the discretion of the board of directors or the compensation committee) and a discretionary annual cash bonus between 20% and 60% of, with a target amount equal to 40%, of Dr. Marshall s then effective base salary (subject to review and adjustment in the sole discretion of the board of directors). Dr. Marshall is also eligible to participate in, subject to applicable eligibility requirements, all of Miragen s benefits plans and fringe benefits and programs that may be provided to senior executives of Miragen from time to time. In connection with Dr. Marshall entering into his 2008 employment agreement, and pursuant to the terms thereof, Miragen issued to Dr. Marshall a stock option exercisable for 164,726 shares of Miragen s common stock on July 31, 2008 with an exercise price of $0.40 per share.

Dr. Marshall s 2008 employment agreement provides that either party may terminate the agreement at-will. In addition, the agreement provides that if Miragen terminates Dr. Marshall s employment without cause or Dr. Marshall resigns for good reason, Dr. Marshall will be eligible to receive the following severance benefits: (i) an amount equal to 12 months of his annual base salary, less applicable deductions, payable in accordance with Miragen s normal payroll schedule; (ii) the vesting of the equivalent of 12 months on all of Dr. Marshall s then outstanding stock options or other equity awards; and (iii) 12 months of continued health coverage. Although, if such termination or resignation occurs within one month prior to or thirteen months following a change of control, Dr. Marshall will be eligible to receive the following severance benefits: (i) an amount equal to 24 months of his annual base salary, less applicable deductions, payable in accordance with Miragen s normal payroll schedule; (ii) the vesting in full of all of his then outstanding stock options or other equity awards then outstanding and subject to time-based vesting; and (iii) 24 months of continued health coverage.

The following definitions have been adopted in Dr. Marshall s 2008 employment agreement:

> cause means (i) Dr. Marshall s commission of any felony or any crime involving fraud, dishonesty or moral turpitude under the laws of the United States or any state thereof; (ii) Dr. Marshall s attempted commission of, or participation in, a fraud or act of dishonesty against Miragen; (iii) Dr. Marshall s intentional, material violation of any contract or agreement between Dr. Marshall and Miragen or any statutory duty Dr. Marshall owes to Miragen, in each case, which remains uncured for 30 days after Miragen provides Dr. Marshall with written notice of his intentional action or conduct; (iv) Dr. Marshall s unauthorized use or disclosure of Miragen s confidential information or trade secrets, which remains uncured for 30 days after Miragen provides Dr. Marshall with written notice of his unauthorized action or conduct; or (v) Dr. Marshall s gross misconduct.

> good reason means the occurrence, without Dr. Marshall s consent, of any one or more of the following: (i) an assignment to Dr. Marshall of any duties or responsibilities that results in a material diminution in Dr.

Marshall s function; (ii) a material reduction in his base salary, subject to specified exception; (iii) the material failure by Miragen to continue Dr. Marshall s participations in any benefit plan or program in which Dr. Marshall was participating; (iv) a relocation of Dr. Marshall s business office to a location that increases Dr. Marshall s one-way commute by more than twenty-five miles; or (v) a material breach by Miragen of any material agreement with Dr. Marshall concerning the terms and conditions of his employment. In order to constitute good reason, however, Dr. Marshall must provide notice to Miragen within 90 days of the existence of the condition or event constituting good reason, after which Miragen has 30 days to cure the condition or event constituting good reason. If

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Miragen fails to cure, Dr. Marshall s separation from service must take place within two years following the initial existence of the good reason condition.

2016 Employment Agreement. In December 2016, Miragen entered into an employment agreement with Dr. Marshall to be effective upon the closing of the Merger, which will supersede his 2008 employment agreement. Under this employment agreement, Dr. Marshall is entitled to an annual base salary (subject to periodic review and adjustment by the board of directors or compensation committee of the board of directors) of $400,000 and a discretionary annual cash bonus equal to 50% of Dr. Marshall s then effective base salary (subject to review and adjustment in the sole discretion of the board of directors or the compensation committee of the board of directors). Dr. Marshall is also eligible to participate in, subject to applicable eligibility requirements, all of Miragen s benefits plans and fringe benefits and programs that may be provided to senior executives of Miragen from time to time.

The 2016 employment agreement provides that either party may terminate the agreement at-will. In addition, the agreement provides that if Miragen terminates Dr. Marshall s employment without cause or Dr. Marshall resigns for good reason, Dr. Marshall will be eligible to receive the following severance benefits: (i) an amount equal to 12 months of his annual base salary, less applicable deductions, payable in accordance with Miragen s normal payroll schedule; (ii) the vesting of the equivalent of 12 months on all of Dr. Marshall s stock options or other equity awards that were outstanding as of the effective date of Dr. Marshall s 2016 employment agreement; and (iii) 12 months of continued health coverage. Although, if such termination or resignation occurs within one month prior to or 12 months following a change of control, Dr. Marshall will be eligible to receive the following severance benefits: (i) an amount equal to 24 months of his annual base salary, less applicable deductions, payable in accordance with Miragen s normal payroll schedule; (ii) the vesting in full of all of his then outstanding stock options or other equity awards then outstanding and subject to time-based vesting; and (iii) 12 months of continued health coverage.

The following definitions have been adopted in each of Dr. Marshall s 2016 employment agreements:

cause means (i) Dr. Marshall s commission of any felony or any crime involving fraud, dishonesty or moral turpitude under the laws of the United States or any state thereof; (ii) Dr. Marshall s attempted commission of, or participation in, a fraud or act of dishonesty against Miragen; (iii) Dr. Marshall s intentional, material violation of any contract or agreement between Dr. Marshall and Miragen or any statutory duty Dr. Marshall owes to Miragen, in each case, which remains uncured for 30 days after Miragen provides written notice of such action or conduct to Dr. Marshall; (iv) Dr. Marshall s unauthorized use or disclosure of Miragen s confidential information or trade secrets; or (v) Dr. Marshall s gross misconduct which remains uncured for 30 days after Miragen provides written notice of such action or conduct to Dr. Marshall.

good reason means the occurrence, without Dr. Marshall s consent, of any one or more of the following: (i) a material reduction in his base salary of ten percent or more (unless such reduction is pursuant to a salary reduction program applicable generally to Miragen s similarly situated executives); (ii) a material reduction in Dr. Marshall s authority, duties or responsibilities; (iii) a relocation of Dr. Marshall s principal place of employment to a place that increases Dr. Marshall s one-way commute by more than 25 miles; or (iv) material breach by Miragen of any material provision of Dr. Marshall s employment agreement.

All severance benefits payable to Dr. Marshall under either his 2008 employment agreement or 2016 employment agreement are subject to him signing, not revoking and complying with a release of claims.

Adam S. Levy

Offer Letter. In April 2016, Miragen entered into an offer letter with Mr. Levy, its chief business officer. The offer letter provides that if Miragen terminates Mr. Levy s employment without cause or Mr. Levy resigns for

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good reason, Mr. Levy will be eligible to receive the following severance benefits: (i) an amount equal to 12 months of his annual base salary, less applicable deductions, payable in accordance with Miragen s normal payroll schedule; (ii) the vesting of the equivalent of 12 months on all of Mr. Levy s then outstanding stock options or other equity awards; and (iii) 12 months of continued health coverage.

The following definitions have been adopted in Mr. Levy s offer letter:

cause means the occurrence of any one or more of the following: (i) Mr. Levy s commission of any felony or any crime involving fraud, dishonesty or moral turpitude under the laws of the United States or any state thereof; (ii) Mr. Levy s attempted commission of, or participation in, a fraud or act of dishonesty against Miragen; (iii) Mr. Levy s material violation of any contract or agreement between Mr. Levy and Miragen or any statutory duty Mr. Levy owes to Miragen, in each case, which remains uncured for 30 days after Miragen provides Mr. Levy notice of such action or conduct; (iv) Mr. Levy s unauthorized use or disclosure of Miragen s confidential information or trade secrets, which remains uncured for 30 days after Miragen provides Mr. Levy notice of such action or conduct; or (v) Mr. Levy s gross misconduct.

good reason means the occurrence, without Mr. Levy s express written consent, of any one or more of the following: (i) the assignment to Mr. Levy of any duties or responsibilities that results in a material diminution in his function; (ii) a material reduction in his base salary, subject to a specified exception; (iii) the material failure by Miragen to continue Mr. Levy s participations in any benefit plan or program in which Mr. Levy was participating, or the taking of any action by Miragen that would materially diminish either Mr. Levy s participation in or benefits received under any existing benefit plan or program; (iv) a relocation of Mr. Levy s business office of employment to a location that increases Mr. Levy s one-way commute by more than twenty-five miles; or (v) material breach by Miragen of any material agreement with Mr. Levy s concerning the terms and conditions of his employment.

2016 Employment Agreement. In December 2016, Miragen entered into an employment agreement with Mr. Levy to be effective upon the closing of the Merger, which will supersede his offer letter. Under this employment agreement, Mr. Levy is entitled to an annual base salary (subject to periodic review and adjustment by the board of directors or compensation committee of the board of directors) of $300,000 and a discretionary annual cash bonus equal to 40% of Mr. Levy s then effective base salary (subject to review and adjustment in the sole discretion of the board of directors or the compensation committee of the board of directors). Mr. Levy is also eligible to participate in, subject to applicable eligibility requirements, all of Miragen s benefits plans and fringe benefits and programs that may be provided to senior executives of Miragen from time to time.

The employment agreement provides that either party may terminate the agreement at-will. In addition, the agreement provides that if Miragen terminates Mr. Levy s employment without cause or Mr. Levy resigns for good reason, Mr. Levy will be eligible to receive the following severance benefits: (i) an amount equal to 12 months of his annual base salary, less applicable deductions, payable in accordance with Miragen s normal payroll schedule; (ii) the vesting of the equivalent of 12 months on all of Mr. Levy s stock options or other equity awards that were outstanding as of the effective date of Mr. Levy s employment agreement; and (iii) 12 months of continued health coverage. Although, if such termination or resignation occurs within one month prior to or 12 months following a change of control, Mr. Levy will be eligible to receive the following severance benefits: (i) an amount equal to 12 months of his annual base salary, less applicable deductions, payable in accordance with Miragen s normal payroll schedule; (ii) the vesting in full of all of Mr. Levy s then outstanding stock options or other equity awards subject to time-based vesting; and (iii) twelve months of continued health coverage.

The following definitions have been adopted in each of Mr. Levy s 2016 employment agreements:

cause means (i) Mr. Levy s commission of any felony or any crime involving fraud, dishonesty or moral turpitude under the laws of the United States or any state thereof; (ii) Mr. Levy s attempted

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commission of, or participation in, a fraud or act of dishonesty against Miragen; (iii) Mr. Levy s intentional, material violation of any contract or agreement between Mr. Levy and Miragen or any statutory duty Mr. Levy owes to Miragen, in each case, which remains uncured for 30 days after Miragen provides written notice of such action or conduct to Mr. Levy; (iv) Mr. Levy s unauthorized use or disclosure of Miragen s confidential information or trade secrets; or (v) Mr. Levy s gross misconduct which remains uncured for 30 days after Miragen provides written notice of such action or conduct to Mr. Levy.

good reason means the occurrence, without Mr. Levy s consent, of any one or more of the following: (i) a material reduction in his base salary of ten percent or more (unless such reduction is pursuant to a salary reduction program applicable generally to Miragen s similarly situated executives); (ii) a material reduction in Mr. Levy s authority, duties or responsibilities; (iii) a relocation of Mr. Levy s principal place of employment to a place that increases Mr. Levy s one-way commute by more than 25 miles; or (iv) material breach by Miragen of any material provision of Mr. Levy s employment agreement.

All severance benefits payable to Mr. Levy under either his offer letter or employment agreement are subject to him signing, not revoking and complying with a release of claims.

Paul D. Rubin, M.D.

Offer Letter. In October 2016, Miragen entered into a severance agreement with Dr. Rubin, its executive vice president, research and development. The offer letter provides that if Miragen terminates Dr. Rubin s employment without cause or Dr. Rubin resigns for good reason, Dr. Rubin will be eligible to receive the following severance benefits: (i) an amount equal to 12 months of his annual base salary, less applicable deductions, payable in accordance with Miragen s normal payroll schedule; (ii) the vesting of the equivalent of 12 months on all of Dr. Rubin s then outstanding stock options or other equity awards; and (iii) 12 months of continued health coverage.

The following definitions have been adopted in Dr. Rubin s offer letter:

cause means the occurrence of any one or more of the following: (i) Dr. Rubin s commission of any felony or any crime involving fraud, dishonesty or moral turpitude under the laws of the United States or any state thereof; (ii) Dr. Rubin s attempted commission of, or participation in, a fraud or act of dishonesty against Miragen; (iii) Dr. Rubin s material violation of any contract or agreement between Dr. Rubin and Miragen or any statutory duty Dr. Rubin owes to Miragen, in each case, which remains uncured for 30 days after Miragen provides Dr. Rubin notice of such action or conduct; (iv) Dr. Rubin s unauthorized use or disclosure of Miragen s confidential information or trade secrets, which remains uncured for 30 days after Miragen provides Dr. Rubin notice of such action or conduct; or (v) Dr. Rubin s gross misconduct.

good reason means the occurrence, without Dr. Rubin s express written consent, of any one or more of the following: (i) the assignment to Dr. Rubin of any duties or responsibilities that results in a material diminution in his function; (ii) a material reduction in his base salary, subject to a specified exception; (iii) the material failure by Miragen to continue Dr. Rubin s participations in any benefit plan or program in which Dr. Rubin was participating, or the taking of any action by Miragen that would materially diminish either Dr. Rubin s participation in or benefits received under any existing benefit plan or program; (iv) a relocation of Dr. Rubin s business office of employment to a location that increases Dr. Rubin s one-way commute by more than twenty-five miles; or (v) material breach by Miragen of any material agreement with

Dr. Rubin s concerning the terms and conditions of his employment.

2016 Employment Agreement. In December 2016, Miragen entered into an employment agreement with Dr. Rubin to be effective upon the closing of the Merger, which will supersede his offer letter. Under this

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employment agreement, Dr. Rubin is entitled to an annual base salary (subject to periodic review and adjustment by the board of directors or compensation committee of the board of directors) of $395,000 and a discretionary annual cash bonus equal to 40% of Dr. Rubin s then effective base salary (subject to review and adjustment in the sole discretion of the board of directors or the compensation committee of the board of directors). Dr. Rubin is also eligible to participate in, subject to applicable eligibility requirements, all of Miragen s benefits plans and fringe benefits and programs that may be provided to senior executives of Miragen from time to time.

The employment agreement provides that either party may terminate the agreement at-will. In addition, the agreement provides that if Miragen terminates Dr. Rubin s employment without cause or Dr. Rubin resigns for good reason, Dr. Rubin will be eligible to receive the following severance benefits: (i) an amount equal to 12 months of his annual base salary, less applicable deductions, payable in accordance with Miragen s normal payroll schedule; (ii) the vesting of the equivalent of 12 months on all of Dr. Rubin s stock options or other equity awards that were outstanding as of the effective date of Dr. Rubin s employment agreement; and (iii) 12 months of continued health coverage. Although, if such termination or resignation occurs within one month prior to or 12 months following a change of control, Dr. Rubin will be eligible to receive the following severance benefits: (i) an amount equal to 12 months of his annual base salary, less applicable deductions, payable in accordance with Miragen s normal payroll schedule; (ii) the vesting in full of all of Dr. Rubin s then outstanding stock options or other equity awards subject to time-based vesting; and (iii) twelve months of continued health coverage.

The following definitions have been adopted in each of Dr. Rubin s 2016 employment agreements:

> cause means (i) Dr. Rubin s commission of any felony or any crime involving fraud, dishonesty or moral turpitude under the laws of the United States or any state thereof; (ii) Dr. Rubin s attempted commission of, or participation in, a fraud or act of dishonesty against Miragen; (iii) Dr. Rubin s intentional, material violation of any contract or agreement between Dr. Rubin and Miragen or any statutory duty Dr. Rubin owes to Miragen, in each case, which remains uncured for 30 days after Miragen provides written notice of such action or conduct to Dr. Rubin; (iv) Dr. Rubin s unauthorized use or disclosure of Miragen s confidential information or trade secrets; or (v) Dr. Rubin s gross misconduct which remains uncured for 30 days after Miragen provides written notice of such action or conduct to Dr. Rubin.

> good reason means the occurrence, without Dr. Rubin s consent, of any one or more of the following: (i) a material reduction in his base salary of ten percent or more (unless such reduction is pursuant to a salary reduction program applicable generally to Miragen s similarly situated executives); (ii) a material reduction in Dr. Rubin s authority, duties or responsibilities; (iii) a relocation of Dr. Rubin s principal place of employment to a place that increases Dr. Rubin s one-way commute by more than 25 miles; or (iv) material breach by Miragen of any material provision of Dr. Rubin s employment agreement.

All severance benefits payable to Dr. Rubin under either his offer letter or employment agreement are subject to him signing, not revoking and complying with a release of claims.

In December 2016, Miragen entered into an employment agreement with Mr. Leverone with substantially the same severance benefits as those provided in Mr. Levy s and Dr. Rubin s employment agreements.

Compensation Risk Management

Miragen has considered the risk associated with its compensation policies and practices for all employees and believes it has designed its compensation policies and practices in a manner that does not create incentives that could lead to excessive risk taking that would have a material adverse effect on Miragen.

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Employment Benefits Plan

2016 Plan

The following description of the 2016 Plan is a summary only and is qualified in its entirety by reference to the complete text of the 2016 Plan. Stockholders are urged to read the actual text of the 2016 Plan in its entirety.

Purpose

The 2016 Plan is designed to secure and retain the services of the combined company s employees, directors and consultants, provide incentives for such, directors and consultants to exert maximum efforts for the success of the combined company and its affiliates, and provide a means by which the combined company s employees, directors and consultants may be given an opportunity to benefit from increases in the value of its common stock. If the 2016 Plan is approved by Signal stockholders, no additional awards will be granted under the 2014 Plan or the Miragen 2008 Plan following the effective date of the 2016 Plan.

Types of Awards

The terms of the 2016 Plan provide for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, other stock awards, and performance awards that may be settled in cash, stock, or other property.

Shares Available for Awards

Subject to adjustment for specified changes in the combined company s capitalization and the reverse stock split, the Share Reserve will not exceed 4,182,404 shares, which number is the sum of (i) 1,681,294 shares, plus (ii) the number of shares subject to outstanding stock awards that were granted under the Miragen 2008 Plan that, from and after the closing date of the Merger, expire or terminate for any reason prior to exercise or settlement, are forfeited because of the failure to meet a contingency or condition required to vest such shares, or are reacquired, withheld or not issued to satisfy a tax withholding obligation in connection with an award or to satisfy the purchase price or exercise price of a stock award, if any, as such shares become available from time to time. In addition, the share reserve will automatically increase on January 1st of each year, for a period of not more than ten years, commencing on January 1st of the year following the year in which the effective date of the 2016 Plan occurs, and ending on (and including) January 1, 2026, in an amount equal to 4% of the shares of common stock outstanding on December 31st of the preceding calendar year; however the board of directors or compensation committee may act prior to January 1st of a given year to provide that there will be no January 1st increase in the share reserve for such year or that the increase in the share reserve for such year will be a lesser number of shares of common stock than would otherwise occur pursuant to the automatic increase.

The following shares of common stock will become available again for issuance under the 2016 Plan: (i) any shares subject to a stock award that are not issued because such stock award expires or otherwise terminates without all of the shares covered by such stock award having been issued; (ii) any shares subject to a stock award that are not issued because such stock award is settled in cash; (iii) any shares issued pursuant to a stock award that are forfeited back to or repurchased by Signal because of the failure to meet a contingency or condition required for the vesting of such shares; and (iv) any shares reacquired by the combined company in satisfaction of tax withholding obligations on a stock award or as consideration for the exercise or purchase price of a stock award.

Eligibility

All of the combined company s (including its affiliates) approximately 45 employees and six non-employee directors as of December 31, 2016 will be eligible to participate in the 2016 Plan following the closing of the Merger and may receive all types of awards other than incentive stock options. Incentive stock options may be granted under the 2016 Plan only to the combined company s employees (including officers) and employees of its affiliates.

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Section 162(m) Limits

Under the 2016 Plan, subject to adjustment for specified changes in the combined company s capitalization and the reverse stock split, no participant will be eligible to be granted performance-based compensation during any calendar year more than: (i) a maximum of 1,500,000 shares of common stock subject to stock options and stock appreciation rights whose value is determined by reference to an increase over an exercise or strike price of at least 100% of the fair market value of a share of common stock on the date of grant; (ii) a maximum of 1,500,000 shares of common stock subject to performance stock awards; and (iii) a maximum of $3,000,000 subject to performance cash awards. These limits are designed to allow the combined company to grant awards that are intended to be exempt from the $1 million limitation on the income tax deductibility of compensation paid per covered employee imposed by Section 162(m) of the Code, and will not apply to awards that the combined company s board of directors determines will not be treated as performance-based compensation.

Non-Employee Director Compensation Limit

Under the 2016 Plan, the maximum number of shares of Signal common stock subject to stock awards granted under the 2016 Plan or otherwise during any one calendar year to any non-employee director, taken together with any cash fees paid by the combined company to such non-employee director during such calendar year for services on its board of directors, will not exceed $500,000 in total value (calculating the value of any such stock awards based on the grant date fair value of such stock awards for financial reporting purposes), or, with respect to the calendar year in which a non-employee director is first appointed or elected to the combined company s board of directors, $1,000,000.

Administration

The 2016 Plan will be administered by the combined company s board of directors, which may in turn delegate authority to administer the 2016 Plan to a committee. The combined company s board of directors will delegate concurrent authority to administer the 2016 Plan to its compensation committee, but may, at any time, revest in itself some or all of the power delegated to its compensation committee. The combined company s board of directors and its compensation committee are each considered to be a Plan Administrator for purposes of this Signal Proposal No. 4. Subject to the terms of the 2016 Plan, the Plan Administrator may determine the recipients, the types of awards to be granted, the number of shares of common stock subject to or the cash value of awards, and the terms and conditions of awards granted under the 2016 Plan, including the period of their exercisability and vesting. The Plan Administrator also has the authority to provide for accelerated exercisability and vesting of awards. Subject to the limitations set forth below, the Plan Administrator also determines the fair market value applicable to a stock award and the exercise or strike price of stock options and stock appreciation rights granted under the 2016 Plan.

The Plan Administrator may also delegate to one or more officers the authority to designate employees who are not officers to be recipients of certain stock awards and the number of shares of common stock subject to such stock awards. Under any such delegation, the Plan Administrator will specify the total number of shares of common stock that may be subject to the stock awards granted by such officer. The officer may not grant a stock award to himself or herself.

Repricing; Cancellation and Re-Grant of Stock Awards

Under the 2016 Plan, the Plan Administrator does not have the authority to reprice any outstanding stock option or stock appreciation right by reducing the exercise or strike price of the stock option or stock appreciation right or to cancel any outstanding stock option or stock appreciation right that has an exercise or strike price greater than the then-current fair market value of a share of common stock in exchange for cash or other stock awards without

obtaining the approval of the combined company s stockholders. Such approval must be obtained within 12 months prior to such an event.

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Stock Options

Stock options may be granted under the 2016 Plan pursuant to stock option agreements. The 2016 Plan permits the grant of stock options that are intended to qualify as ISOs and NSOs.

The exercise price of a stock option granted under the 2016 Plan may not be less than 100% of the fair market value of the common stock subject to the stock option on the date of grant and, in some cases (see *Limitations on Incentive Stock Options* below), may not be less than 110% of such fair market value.

The term of stock options granted under the 2016 Plan may not exceed ten years and, in some cases (see *Limitations on Incentive Stock Options* below), may not exceed five years. Except as otherwise provided in a participant s stock option agreement or other written agreement with the combined company or one of its affiliates, if a participant s service relationship with combined company or any of its affiliates, referred to in this Signal Proposal No. 4 as continuous service, terminates (other than for cause and other than upon the participant s death or disability), the participant may exercise any vested stock options for up to three months following the participant s termination of continuous service. Except as otherwise provided in a participant s stock option agreement or other written agreement with the combined company or one of its affiliates, if a participant s continuous service terminates due to the participant s disability or death (or the participant dies within a specified period, if any, following termination of continuous service), the participant, or his or her beneficiary, as applicable, may exercise any vested stock options for up to 12 months following the participant s termination due to the participant s disability or for up to 18 months following the participant s death. Except as explicitly provided otherwise in a participant s stock option agreement or other written agreement with the combined company or one of its affiliates, if a participant s continuous service is terminated for cause (as defined in the 2016 Plan), all stock options held by the participant will terminate upon the participant s termination of continuous service and the participant will be prohibited from exercising any stock option from and after such termination date. Except as otherwise provided in a participant s stock option agreement or other written agreement with the combined company or one of its affiliates, the term of a stock option may be extended if the exercise of the stock option following the participant s termination of continuous service (other than for cause and other than upon the participant s death or disability) would be prohibited by applicable securities laws or if the sale of any common stock received upon exercise of the stock option following the participant s termination of continuous service (other than for cause) would violate Signal s insider trading policy. In no event, however, may a stock option be exercised after its original expiration date.

Acceptable forms of consideration for the purchase of common stock pursuant to the exercise of a stock option under the 2016 Plan will be determined by the Plan Administrator and may include payment: (i) by cash, check, bank draft or money order payable to the combined company; (ii) pursuant to a program developed under Regulation T as promulgated by the Federal Reserve Board; (iii) by delivery to the combined company of shares of common stock (either by actual delivery or attestation); (iv) by a net exercise arrangement (for NSOs only); or (v) in other legal consideration approved by the Plan Administrator.

Stock options granted under the 2016 Plan may vest as determined by the Plan Administrator at the rate specified in the stock option agreement. Shares covered by different stock options granted under the 2016 Plan may be subject to different vesting schedules as the Plan Administrator may determine.

The Plan Administrator may impose limitations on the transferability of stock options granted under the 2016 Plan in its discretion. Generally, a participant may not transfer a stock option granted under the 2016 Plan other than by will or the laws of descent and distribution or, subject to approval by the Plan Administrator, pursuant to a domestic relations order or an official marital settlement agreement. However, the Plan Administrator may permit transfer of a stock option in a manner that is not prohibited by applicable tax and securities laws. In addition, subject to approval

by the Plan Administrator, a participant may designate a beneficiary who may exercise the stock option following the participant s death.

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Limitations on Incentive Stock Options

The aggregate fair market value, determined at the time of grant, of shares of common stock with respect to ISOs that are exercisable for the first time by a participant during any calendar year under all of the combined company s stock plans may not exceed $100,000. The stock options or portions of stock options that exceed this limit or otherwise fail to qualify as ISOs are treated as NSOs. No ISO may be granted to any person who, at the time of grant, owns or is deemed to own stock possessing more than 10% of Signal s total combined voting power or that of any affiliate unless the following conditions are satisfied:

- the exercise price of the ISO must be at least 110% of the fair market value of the common stock subject to the ISO on the date of grant; and
- the term of the ISO must not exceed five years from the date of grant.

Subject to adjustment for specified changes in capitalization and the reverse stock split, the aggregate maximum number of shares of common stock that may be issued pursuant to the exercise of ISOs under the 2016 Plan is 20,912,020 shares.

Stock Appreciation Rights

Stock appreciation rights may be granted under the 2016 Plan pursuant to stock appreciation right agreements. Each stock appreciation right is denominated in common stock share equivalents. The strike price of each stock appreciation right will be determined by the Plan Administrator, but will in no event be less than 100% of the fair market value of the common stock subject to the stock appreciation right on the date of grant. The Plan Administrator may also impose restrictions or conditions upon the vesting of stock appreciation rights that it deems appropriate. The appreciation distribution payable upon exercise of a stock appreciation right may be paid in shares of Signal common stock, in cash, in a combination of cash and stock, or in any other form of consideration determined by the Plan Administrator and set forth in the stock appreciation right agreement. Stock appreciation rights will be subject to the same conditions upon termination of continuous service and restrictions on transfer as stock options under the 2016 Plan.

Restricted Stock Awards

Restricted stock awards may be granted under the 2016 Plan pursuant to restricted stock award agreements. A restricted stock award may be granted in consideration for cash, check, bank draft or money order payable to the combined company, the participant s services performed for the combined company or any of its affiliates, or any other form of legal consideration acceptable to the Plan Administrator. Shares of common stock acquired under a restricted stock award may be subject to forfeiture to or repurchase by the combined company in accordance with a vesting schedule to be determined by the Plan Administrator. Rights to acquire shares of common stock under a restricted stock award may be transferred only upon such terms and conditions as are set forth in the restricted stock award agreement. A restricted stock award agreement may provide that any dividends paid on restricted stock will be subject to the same vesting conditions as apply to the shares subject to the restricted stock award. Upon a participant s termination of continuous service for any reason, any shares subject to restricted stock awards held by the participant that have not vested as of such termination date may be forfeited to or repurchased by the combined company.

Restricted Stock Unit Awards

Restricted stock unit awards may be granted under the 2016 Plan pursuant to restricted stock unit award agreements. Payment of any purchase price may be made in any form of legal consideration acceptable to the Plan Administrator. A restricted stock unit award may be settled by the delivery of shares of Signal common stock, in cash, in a combination of cash and stock, or in any other form of consideration determined by the Plan Administrator and set forth in the restricted stock unit award agreement. Restricted stock unit awards may be

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subject to vesting in accordance with a vesting schedule to be determined by the Plan Administrator. Dividend equivalents may be credited in respect of shares of common stock covered by a restricted stock unit award, provided that any additional shares credited by reason of such dividend equivalents will be subject to all of the same terms and conditions of the underlying restricted stock unit award. Except as otherwise provided in a participant s restricted stock unit award agreement or other written agreement with the combined company or one of its affiliates, restricted stock units that have not vested will be forfeited upon the participant s termination of continuous service for any reason.

Performance Awards

The 2016 Plan allows the combined company to grant performance stock and cash awards, including such awards that may qualify as performance-based compensation that is not subject to the $1 million limitation on the income tax deductibility of compensation paid per covered employee imposed by Section 162(m) of the Code.

A performance stock award is a stock award that is payable (including that may be granted, may vest, or may be exercised) contingent upon the attainment of pre-determined performance goals during a performance period. A performance stock award may require the completion of a specified period of continuous service. The length of any performance period, the performance goals to be achieved during the performance period, and the measure of whether and to what degree such performance goals have been attained will be determined by the compensation committee of the combined company s board of directors, except that the Plan Administrator also may make any such determinations to the extent that the award is not intended to qualify as performance-based compensation under Section 162(m) of the Code. In addition, to the extent permitted by applicable law and the performance stock award agreement, the Plan Administrator may determine that cash may be used in payment of performance stock awards.

A performance cash award is a cash award that is payable contingent upon the attainment of pre-determined performance goals during a performance period. A performance cash award may require the completion of a specified period of continuous service. The length of any performance period, the performance goals to be achieved during the performance period, and the measure of whether and to what degree such performance goals have been attained will be determined by the compensation committee of the combined company s board of directors, except that the Plan Administrator also may make any such determinations to the extent that the award is not intended to qualify as performance-based compensation under Section 162(m) of the Code. The Plan Administrator may specify the form of payment of performance cash awards, which may be cash or other property, or may provide for a participant to have the option for his or her performance cash award to be paid in cash or other property.

In granting a performance stock or cash award intended to qualify as performance-based compensation under Section 162(m) of the Code, the compensation committee of the combined company s board of directors will set a period of time, or a performance period, over which the attainment of one or more goals, or performance goals, will be measured. Within the time period prescribed by Section 162(m) of the Code (no later than the earlier of the 90th day of a performance period and the date on which 25% of the performance period has elapsed, and in any event at a time when the achievement of the performance goals remains substantially uncertain), the compensation committee of the combined company s board of directors will establish the performance goals, based upon one or more criteria, or performance criteria, enumerated in the 2016 Plan and described below. As soon as administratively practicable following the end of the performance period, the compensation committee of the combined company s board of directors will certify in writing whether the performance goals have been satisfied.

Performance goals under the 2016 Plan will be based on any one or more of the following performance criteria: (i) earnings (including earnings per share and net earnings); (ii) earnings before interest, taxes and depreciation; (iii) earnings before interest, taxes, depreciation and amortization; (iv) earnings before interest, taxes, depreciation, amortization and legal settlements; (v) earnings before interest, taxes, depreciation,

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amortization, legal settlements and other income (expense); (vi) earnings before interest, taxes, depreciation, amortization, legal settlements, other income (expense) and stock-based compensation; (vii) earnings before interest, taxes, depreciation, amortization, legal settlements, other income (expense), stock-based compensation and changes in deferred revenue; (viii) earnings before interest, taxes, depreciation, amortization, legal settlements, other income (expense), stock-based compensation, other non-cash expenses and changes in deferred revenue; (ix) total stockholder return; (x) return on equity or average stockholder s equity; (xi) return on assets, investment, or capital employed; (xii) stock price; (xiii) margin (including gross margin); (xiv) income (before or after taxes); (xv) operating income; (xvi) operating income after taxes; (xvii) pre-tax profit; (xviii) operating cash flow; (xix) sales or revenue targets; (xx) increases in revenue or product revenue; (xxi) expenses and cost reduction goals; (xxii) improvement in or attainment of working capital levels; (xxiii) economic value added (or an equivalent metric); (xxiv) market share; (xxv) cash flow; (xxvi) cash flow per share; (xxvii) cash balance; (xxviii) cash burn; (xxix) cash collections; (xxx) share price performance; (xxxi) debt reduction; (xxxii) implementation or completion of projects or processes (including, without limitation, clinical trial initiation, clinical trial enrollment and dates, clinical trial results, regulatory filing submissions, regulatory filing acceptances, regulatory or advisory committee interactions, regulatory approvals, new and supplemental indications for existing products, and product supply); (xxxiii) stockholders equity; (xxxiv) capital expenditures; (xxxv) debt levels; (xxxvi) operating profit or net operating profit; (xxxvii) workforce diversity; (xxxviii) growth of net income or operating income; (xxxix) billings; (xl) bookings; (xli) employee retention; (xlii) initiation of phases of clinical trials and/or studies by specific dates; (xliii) acquisition of new customers, including institutional accounts; (xliv) customer retention and/or repeat order rate; (xlv) number of institutional customer accounts (xlvi) budget management; (xlvii) improvements in sample and test processing times; (xlviii) regulatory milestones; (xlix) progress of internal research or clinical programs; (l) progress of partnered programs; (li) partner satisfaction; (lii) milestones related to samples received and/or tests run; (liii) expansion of sales in additional geographies or markets; (liv) research progress, including the development of programs; (lv) submission to, or approval by, a regulatory body (including, but not limited to the U.S. Food and Drug Administration) of an applicable filing or a product; (lvi) timely completion of clinical trials; (lvii) milestones related to samples received and/or tests or panels run; (lviii) expansion of sales in additional geographies or markets; (lix) research progress, including the development of programs; (lx) patient samples processed and billed; (lxi) sample processing operating metrics (including, without limitation, failure rate maximums and reduction of repeat rates); (lxii) strategic partnerships or transactions (including in-licensing and out-licensing of intellectual property); (lxiii) pre-clinical development related to compound goals; (lxiv) customer satisfaction; and (lxv) and to the extent that an award is not intended to comply with Section 162(m) of the Code, other measures of performance selected by the board of directors of the combined company.

Performance goals may be based on a company-wide basis, with respect to one or more business units, divisions, affiliates or business segments, and in either absolute terms or relative to the performance of one or more comparable companies or the performance of one or more relevant indices. The compensation committee of the combined company s board of directors (or, to the extent that an award is not intended to qualify as performance-based compensation under Section 162(m) of the Code, the Plan Administrator) is authorized to make appropriate adjustments in the method of calculating the attainment of performance goals for a performance period as follows; *provided, however*, that to the extent that an award is intended to qualify as performance-based compensation under Section 162(m) of the Code, any such adjustment may be made only if such adjustment is objectively determinable and specified in the award agreement at the time the award is granted or in such other document setting forth the performance goals for the award at the time the performance goals are established: (i) to exclude restructuring and/or other nonrecurring charges; (ii) to exclude exchange rate effects; (iii) to exclude the effects of changes to U.S. GAAP; (iv) to exclude the effects of any statutory adjustments to corporate tax rates; (v) to exclude the effects of items that are unusual in nature or occur infrequently as determined under U.S. GAAP; (vi) to exclude the dilutive effects of acquisitions or joint ventures; (vii) to assume that any business divested by the combined company achieved performance objectives at targeted levels during the balance of a performance period following such divestiture; (viii)

to exclude the effect of any change in the outstanding shares of common stock of the combined company by reason of any stock dividend or split, stock repurchase, reorganization, recapitalization, merger, consolidation, spin-off, combination or exchange

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of shares or other similar corporate change, or any distributions to common stockholders other than regular cash dividends; (ix) to exclude the effects of stock based compensation and the award of bonuses under the combined company s bonus plans; (x) to exclude costs incurred in connection with potential acquisitions or divestitures that are required to be expensed under U.S. GAAP; and (xi) to exclude the goodwill and intangible asset impairment charges that are required to be recorded under U.S. GAAP.

In addition, the compensation committee of the combined company s board of directors (or, to the extent that an award is not intended to qualify as performance-based compensation under Section 162(m) of the Code, the Plan Administrator) retains the discretion to reduce or eliminate the compensation or economic benefit due upon the attainment of any performance goals and to define the manner of calculating the performance criteria it selects to use for a performance period.

Other Stock Awards

Other forms of stock awards valued in whole or in part by reference to, or otherwise based on, common stock may be granted either alone or in addition to other stock awards under the 2016 Plan. The Plan Administrator will have sole and complete authority to determine the persons to whom and the time or times at which such other stock awards will be granted, the number of shares of common stock to be granted and all other terms and conditions of such other stock awards.

Clawback Policy

Awards granted under the 2016 Plan will be subject to recoupment in accordance with any clawback policy that the combined company is required to adopt pursuant to the listing standards of any national securities exchange or association on which Signal s securities are listed or as is otherwise required by the Dodd-Frank Wall Street Reform and Consumer Protection Act or other applicable law. In addition, the Plan Administrator may impose other clawback, recovery or recoupment provisions in an award agreement as the Plan Administrator determines necessary or appropriate, including a reacquisition right in respect of previously acquired shares of common stock or other cash or p