PROSPECTUS



\$75,000,000

Common Stock

We have entered into a certain Sales Agreement, or sales agreement, with Cowen and Company, LLC, or Cowen, relating to shares of our common stock offered by this prospectus. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$75.0 million from time to time through Cowen.

Our common stock is traded on the Nasdaq Global Select Market, or the Exchange, under the symbol "TRVN." On December 11, 2015, the last reported sale price of our common stock was \$10.47 per share.

Sales of our common stock, if any, under this prospectus may be made in sales deemed to be "at-the-market" equity offerings as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act, including sales made directly on or through the Exchange, the existing trading market for our common stock, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices, and/or any other method permitted by law. Cowen is not required to sell any specific number or dollar amount of securities, but will act as a sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between Cowen and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

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

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" on page 4 of this prospectus and under similar headings in the other documents that are incorporated by reference into this prospectus.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

Cowen and Company

The date of this prospectus is January 7, 2015.

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ABOUT THIS PROSPECTUS

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

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

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

Unless otherwise mentioned or unless the context requires otherwise, all references in this prospectus to "Trevena," "company," "we," "us" and "our" or similar references refer to Trevena. Inc.

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

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PROSPECTUS SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus, including the information incorporated by reference in this prospectus, and the information included in any free writing prospectus that we have authorized for use in connection with this offering, including the information under the heading "Risk Factors" in this prospectus on page 4 and in the documents incorporated by reference into this prospectus.

We are a clinical stage biopharmaceutical company focused on the discovery and development of biased ligands targeting G protein coupled receptors.

Using our proprietary discovery platform, we have identified and are developing the following three differentiated product candidates:

Oliceridine (TRV130): In October 2015, we announced that the United States Adopted Name (USAN) approved name for TRV130 is oliceridine. We are developing oliceridine as a first-line treatment for patients experiencing moderate to severe acute pain where IV administration is preferred. We hold a U.S. patent (U.S. Patent No. 8,835,488) covering the composition of matter and methods of use for oliceridine. We have retained all worldwide development and commercialization rights to oliceridine, and plan to commercialize it in the United States for use in acute care settings such as hospitals and ambulatory surgery centers if it receives regulatory approval.

We have completed two Phase 2 clinical trials of oliceridine and we expect to initiate a Phase 3 clinical program in the first quarter of 2016. We will discuss our Phase 3 plans with the FDA at an End of Phase 2 ("EoP2") meeting, which we expect to occur in the first quarter of 2016. At the EoP2 meeting, we will discuss the design and conduct of two adequate and well-controlled clinical studies — one in patients after bunionectomy surgery, and one in patients after abdominoplasty surgery — in which we expect a total of between 300 and 600 patients to be exposed to oliceridine. We expect to begin these studies in the second quarter of 2016. Based on recent draft guidance from the FDA on the development of analgesic drug products, we believe that these two studies, plus additional Phase 3 studies in which approximately 600 to 900 additional patients would be exposed to oliceridine will be sufficient for the FDA to review a new drug application, or NDA, for oliceridine. Assuming FDA's concurrence with these plans, we expect that top-line data from the pivotal trials will be available in the first quarter of 2017. If these trials are successful, we expect to submit an NDA for oliceridine to the FDA in the second half of 2017.

TRV027: We are developing TRV027 for the treatment of acute heart failure, or AHF. In early 2014, we initiated a Phase 2b clinical trial of TRV027 (BLAST-AHF) for the treatment of AHF. In January 2015, we conducted a planned interim analysis, evaluating data from approximately 250 patients in this trial. Upon reviewing the data, the data safety monitoring board, or DSMB, and the BLAST-AHF Steering Committee recommended that future enrollment be weighted to the most promising dose of 5 mg/hr. We announced in March 2015 that remaining enrollment will be weighted 2:1:2:1 to placebo, 1 mg/hr, 5 mg/hr, and 25 mg/hr, respectively, and that we have increased target enrollment in the study from 500 patients to 620 patients. In addition, the DSMB and BLAST-AHF Steering Committee determined that patients with lower baseline systolic blood pressure could safely enroll in the study and we have modified the inclusion criteria accordingly. Allergan plc, which holds an exclusive option to license TRV027, has fully funded this expansion of the study via a \$10.0 million payment to us to defray the external and internal costs of increasing the study sample size. As of October 21, 2015, 446 patients have been enrolled in the trial. The most recent DSMB review of the trial was conducted in October 2015 and the DSMB recommended that the trial continue without modification. We expect to release top-line data from the BLAST-AHF trial in the second quarter of 2016.

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• TRV250: We are developing TRV250, a G protein biased ligand targeting the delta receptor, as a compound with potential first-in-class mechanism for the treatment of migraine. TRV250 also may have utility in a range of other central nervous system indications, and based on target selectivity it is not expected to have the addiction liability of mu opioid drugs like morphine or oxycodone. We have initiated preclinical development activities to support our submission of an investigational new drug application to the U.S. Food and Drug Administration in 2016.

In addition to the above three product candidates, we identified and have completed the Phase 1 program for TRV734, an orally administered clinical compound expected to be used for first-line treatment of moderate to severe acute and chronic pain. We intend to continue to focus our efforts for TRV734 on securing a worldwide development and commercialization partner for this asset. The U.S. patent covering the composition of matter and methods of use for TRV734 was issued in June 2015 (U.S. Patent No. 9,044,469), and we hold all worldwide development and commercialization rights to this asset.

We were incorporated under the laws of the State of Delaware in November 2007. Our principal executive office is located at 1018 West 8th Avenue, Suite A, King of Prussia, Pennsylvania 19406. Our telephone number is (610) 354-8840. Our website address is www.trevenainc.com. The information contained on our website is not incorporated by reference into this prospectus, and you should not consider any information contained on, or that can be accessed through, our website as part of this prospectus or in deciding whether to purchase our common stock.

"Trevena", the Trevena logo and other trademarks or service marks of Trevena, Inc. appearing in this prospectus are the property of Trevena, Inc. This prospectus contains additional trade names, trademarks and service marks of others, which are the property of their respective owners.

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THE OFFERING

Common Stock Offered By Us Shares of our common stock having an aggregate offering price of up to \$75.0 million.

Manner of Offering "At-the-market" offering that may be made from time to time through our sales agent, Cowen. See "Plan of

Distribution" on page 13.

Use of Proceeds We currently intend to use the net proceeds from this offering primarily for research, development,

manufacturing, and commercialization of product candidates, and for other general corporate purposes. See "Use

of Proceeds" on page 6 of this prospectus.

Risk Factors Investing in our common stock involves significant risks. See "Risk Factors" on page 4 of this prospectus, and

under similar headings in other documents incorporated by reference into this prospectus.

NASDAQ Global Select Market Symbol TRVN

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RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully review the risks and uncertainties described below and under the section titled "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2014, as updated by our annual, quarterly and other reports and documents that are incorporated by reference into this prospectus, before deciding whether to purchase any of the securities being registered pursuant to the registration statement of which this prospectus is a part. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or part of your investment. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations. Please also read carefully the section below titled "Special Note Regarding Forward-Looking Statements."

Additional Risks Related to This Offering

You may experience dilution.

The offering price per share in this offering may exceed the net tangible book value per share of our common stock outstanding prior to this offering. Assuming that an aggregate of 7,163,323 shares of our common stock are sold at a price of \$10.47 per share, the last reported sale price of our common stock on the Exchange on December 11, 2015, for aggregate gross proceeds of \$75.0 million, and after deducting commissions and estimated offering expenses payable by us, you would experience immediate dilution of \$6.49 per share, representing the difference between our as adjusted net tangible book value per share as of September 30, 2015 after giving effect to this offering and the assumed offering price. The exercise of outstanding stock options and warrants would result in further dilution of your investment. See the section entitled "Dilution" below for a more detailed illustration of the dilution you would incur if you participate in this offering. Because the sales of the shares offered hereby will be made directly into the market or in negotiated transactions, the prices at which we sell these shares will vary and these variations may be significant. Purchasers of the shares we sell, as well as our existing shareholders, will experience significant dilution if we sell shares at prices significantly below the price at which they invested.

You may experience future dilution as a result of future equity offerings.

To raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering.

Our management might apply the net proceeds from this offering in ways with which you do not agree and in ways that may impair the value of your investment.

We currently intend to use the net proceeds from this offering primarily for research, development, manufacturing, and commercialization of product candidates, and for other general corporate purposes. Pending these uses, we expect to invest the net proceeds in short-term, interest-bearing securities. Our management has broad discretion as to the use of these proceeds and you will be relying on the judgment of our management regarding the application of these proceeds. We might apply these proceeds in ways with which you do not agree, or in ways that do not yield a favorable return. If our management applies these proceeds in a manner that does not yield a significant return, if any, on our investment of these net proceeds, it could compromise our ability to pursue our growth strategy and adversely affect the market price of our common stock.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

offering contain or may contain forward-looking statements within the meaning of Section 27A of the Securities Act, and Section 21E of the Exchange Act, that involve a number of risks and uncertainties. Although our forward-looking statements reflect the good faith judgment of our management, these statements can only be based on facts and factors currently known by us. Consequently, these forward-looking statements are inherently subject to risks and uncertainties, and actual results and outcomes may differ materially from results and outcomes discussed in the forward-looking statements. Forward-looking statements may include, but are not limited to, statements about: our plans to develop and potentially commercialize our product candidates; the exercise by Actavis, Inc. (formerly Forest Laboratories Holdings Limited) of its option to license TRV027 and, if exercised, our ability to achieve milestones under the license; our planned clinical trials and preclinical studies for our product candidates; the timing of and our ability to obtain and maintain regulatory approvals for our product candidates; the extent of clinical trials potentially required by the U.S. Food and Drug Administration for our product candidates; the clinical utility and market acceptance of our product candidates; our commercialization, marketing and manufacturing capabilities and strategy; our intellectual property position; and our ability to identify additional product candidates with significant commercial potential that are consistent with our commercial objectives.

Forward-looking statements can be identified by the use of forward-looking words such as "believes," "expects," "hopes," "may," "will," "plan," "intends," "estimates," "could," "should," "continue," "seeks," "pro forma," or "anticipates," or other similar words (including their use in the negative), or by discussions of future matters such as the development of new products, technology enhancements, possible collaborations and other statements that are not historical. These statements include but are not limited to statements under the captions "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and in other sections incorporated by reference from our Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, as applicable, as well as our other filings with the SEC. You should be aware that the occurrence of any of the events discussed under the heading "Risk Factors" in this prospectus and any documents incorporated by reference herein could substantially harm our business, operating results and financial condition and that if any of these events occurs, it could adversely affect the value of an investment in our securities.

The cautionary statements made in this prospectus are intended to be applicable to all related forward-looking statements wherever they may appear in this prospectus or any documents incorporated by reference herein. We urge you not to place undue reliance on these forward-looking statements, which speak only as of the date they are made. Except as required by law, we assume no obligation to update our forward-looking statements, even if new information becomes available in the future.

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USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$75.0 million from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. We estimate that the net proceeds from the sale of the shares of common stock that we are offering may be up to \$72.7 million, after deducting Cowen's commission and estimated offering expenses payable by us.

We currently intend to use the net proceeds from this offering primarily for research, development, manufacturing, and commercialization of product candidates, and for other general corporate purposes. Pending these uses, we expect to invest the net proceeds in short-term, interest-bearing securities.

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DILUTION

Our net tangible book value as of September 30, 2015 was approximately \$157.7 million, or \$3.11 per share. Net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of September 30, 2015. Dilution with respect to net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering.

After giving effect to the sale of 7,163,323 shares of our common stock in this offering at an assumed offering price of \$10.47 per sharethe last reported sale price of our common stock on the Exchange on December 11, 2015, and after deducting estimated offering commissions and offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2015 would have been approximately \$230.4 million, or \$3.98 per share. This represents an immediate increase in net tangible book value of \$0.87 per share to existing stockholders and immediate dilution of \$6.49 per share to investors purchasing our common stock in this offering at the public offering price. The following table illustrates this dilution on a per share basis:

Assumed public offering price per share		\$	10.47
Net tangible book value per share as of September 30, 2015	\$	3.11	
	6	0.07	
Increase in net tangible book value per share attributable to this offering	\$	0.87	
As adjusted net tangible book value per share as of September 30, 2015, after giving effect to this offering		¢	3.98
As adjusted net tangible book value per share as of september 30, 2013, and giving effect to this offering		Φ	3.90
Dilution per share to investors purchasing our common stock in this offering		\$	6.49

The above discussion and table are based on 50,736,251 shares outstanding as of September 30, 2015, and exclude:

- · 27,839 shares of common stock issuable upon the exercise of warrants outstanding as of September 30, 2015, having a weighted average exercise price of \$6.11 per share;
- 4,657,949 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2015, having a weighted average exercise price of \$4.85 per share; and
- · an aggregate of 1,223,636 shares of common stock reserved for future issuance under our stock option and employee stock purchase plans as of September 30, 2015.

The table above assumes for illustrative purposes that an aggregate of 7,163,323 shares of our common stock are sold during the term of the sales agreement with Cowen at a price of \$10.47 per share, the last reported sale price of our common stock on the Exchange on December 11, 2015, for aggregate gross proceeds of \$75.0 million. The shares subject to the sales agreement with Cowen are being sold from time to time at various prices. An increase of \$2.62 per share in the price at which the shares are sold from the assumed offering price of \$10.47 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$75.0 million during the term of the sales agreement with Cowen is sold at that price, would increase our adjusted net tangible book value per share after the offering to \$4.08 per share and would

increase the dilution in net tangible book value per share to new investors in this offering to \$9.01 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of \$2.62 per share in the price at which the shares are sold from the assumed offering price of \$10.47 per share shown in the table above, assuming all of our common stock in the aggregate amount of

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\$75.0 million during the term of the sales agreement with Cowen is sold at that price, would decrease our adjusted net tangible book value per share after the offering to \$3.82 per share and would decrease the dilution in net tangible book value per share to new investors in this offering to \$4.03 per share, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only.

To the extent that outstanding options or warrants outstanding as of September 30, 2015 have been or may be exercised or other shares issued, investors purchasing our common stock in this offering may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

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DESCRIPTION OF CAPITAL STOCK

As of the date of this prospectus, our amended and restated certificate of incorporation authorizes us to issue 100,000,000 shares of common stock, par value \$0.001 per share and 5,000,000 shares of preferred stock, par value \$0.001 per share. As of December 11, 2015, 50,794,987 shares of common stock were outstanding and no shares of preferred stock were outstanding.

The following summary describes the material terms of our capital stock and the registration rights under our Amended and Restated Investor Rights Agreement, dated as of May 3, 2013, by and among us and certain of our stockholders, which we refer to as out Investor Rights Agreement. The descriptions of capital stock and the registration rights under our Investor Rights Agreement are qualified by reference to our amended and restated certificate of incorporation, our amended and restated bylaws and our Investor Rights Agreement, which are incorporated by reference as exhibits into the registration statement of which this prospectus is a part.

Common Stock

Voting. Our common stock is entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders, including the election of directors, and does not have cumulative voting rights. Accordingly, the holders of a majority of the shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election.

Dividends. Subject to preferences that may be applicable to any then-outstanding preferred stock, the holders of common stock are entitled to receive dividends, if any, as may be declared from time to time by our Board of Directors out of legally available funds.

Liquidation. In the event of our liquidation, dissolution or winding-up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities, subject to the satisfaction of any liquidation preference granted to the holders of any outstanding shares of preferred stock.

Rights and Preferences. Holders of our common stock have no preemptive, conversion or subscription rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of our preferred stock that we may designate and issue in the future.

Fully Paid and Nonassessable. All of our outstanding shares of common stock are fully paid and nonassessable.

Preferred Stock

Under our amended and restated certificate of incorporation, our board of directors has the authority, without further action by stockholders, to designate up to 5,000,000 shares of preferred stock in one or more series and to fix or alter, from time to time, the designations, powers and rights of each series of preferred stock and the qualifications, limitations or restrictions of any series of preferred stock, including dividend rights, dividend rate, conversion rights, voting rights, rights and terms of redemption (including sinking fund provisions), redemption price or prices, and the liquidation preference of any wholly unissued series of preferred stock, any or all of which may be greater than the rights of the common stock, and to establish the number of shares constituting any such series. To date, none of the 5,000,000 authorized shares of preferred stock have been designated by our board of directors.

The laws of the state of Delaware, the state of our incorporation, provide that the holders of preferred stock will have the right to vote separately as a class on any proposal involving fundamental changes in the rights of holders of such preferred stock. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

The issuance of preferred stock could adversely affect the voting power, conversion or other rights of holders of common stock and reduce the likelihood that common stockholders will receive dividend payments and payments upon liquidation. Preferred stock could be issued quickly with terms designed to delay, deter or prevent a change in

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control of our company or make removal of management more difficult. Additionally, the issuance of preferred stock may have the effect of decreasing the market price of our common stock.

Warrants

We have outstanding an immediately exercisable warrant to purchase 20,161 shares of our common stock at an exercise price of \$6.20 per share, which expires in December 2021. We refer to this warrant as the Comerica warrant. We also have outstanding an immediately exercisable warrant to purchase an aggregate of 2,419 shares of our common stock at an exercise price of \$0.06 per share, which warrant expires in June 2018. We refer to this warrant as the SVB warrant. The SVB warrant has a net

exercise provision under which the holder may, in lieu of payment of the exercise price in cash, surrender the warrant and receive a net amount of shares based on the fair market value of our stock at the time of exercise of the warrant after deduction of the aggregate exercise price. Each of the Comerica warrant and the SVB warrant also contain provisions for the adjustment of the exercise price and the number of shares issuable upon the exercise of the warrant in the event of certain stock dividends, stock splits, reorganizations, reclassifications and consolidations. We have also granted registration rights to the SVB and Comerica warrant holders, as more fully described below under "Registration Rights". In connection with entering into a credit facility in September 2014, we issued warrants to purchase 7,678 shares of our common stock at a price of \$5.8610 per share, which expire in September 2024, to Oxford Finance LLC, Square 1 Bank and Three Point Capital, LLC. If we draw additional funds under the facility, we would be required to issue additional warrants to these parties, up to a maximum number of warrants to purchase 126,685 shares of our common stock.

Registration Rights

We and certain holders of our common stock are parties to our Investor Rights Agreement. The registration rights provisions of our Investor Rights Agreement provide those holders with demand and piggyback registration rights with respect to the shares of common stock currently held by them. Pursuant to the terms of the Comerica warrant and the SVB warrant, the holders of such warrants have piggyback registration rights, and, in some cases, demand registration rights with respect to the shares of common stock issuable upon exercise of such warrants on the same terms as are set forth in our Investor Rights Agreement.

Demand Registration Rights. Pursuant to the terms of the investor rights agreement, parties thereto who hold at least 181,452 shares of our common stock in the aggregate have the right to demand that we file up to a total of two registration statements, as long as the anticipated aggregate offering price, net of underwriting discounts and commissions, would exceed \$5,000,000. These registration rights are subject to specified conditions and limitations, including the right of the underwriters, if any, to limit the number of shares included in any such registration under specified circumstances. Upon such a request, we are required to effect the registration as expeditiously as reasonably possible. An aggregate of 15,210,498 shares of common stock are entitled to these demand registration rights.

"Piggyback" Registration Rights. If we propose to register any of our securities under the Securities Act either for our own account or for the account of other stockholders, the holders of registrable securities will each be entitled to notice of the registration and will be entitled to include their shares of common stock in the registration statement. These piggyback registration rights are subject to specified conditions and limitations, including the right of the underwriters to limit the number of shares included in any such registration under specified circumstances. An aggregate of 15,210,498 shares of common stock and 22,580 shares of our common stock issuable upon the exercise of outstanding warrants are entitled to these piggyback registration rights.

Form S-3 Registration Rights. At any time after we become eligible to file a registration statement on Form S-3, holders of registrable securities will be entitled, upon their written request, to have such shares registered by us on a Form S-3 registration statement at our expense, provided that such requested registration has an anticipated aggregate offering size to the public of at least \$1,000,000 and subject to other specified conditions and limitations. Registrations effected on Form S-3 will not reduce the number of demand registrations allowed, as described under "Demand Registration Rights" above. An aggregate of 15,210,498 shares of common stock and 22,580 shares of our common stock issuable upon the exercise of outstanding warrants are entitled to these Form S-3 registration rights.

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Expenses of Registration. We will pay all expenses relating to any demand, piggyback or Form S-3 registration, other than underwriting discounts and commissions, subject to specified conditions and limitations.

Termination of Registration Rights. The registration rights granted under the investor rights agreement will terminate in February 2017 or, if earlier, with respect to a particular holder, at such time as that holder holds less than 1% of our common stock and such holder and its affiliates may sell all of their shares of common stock pursuant to Rule 144 under the Securities Act without any restriction during any 90-day period.

Anti-Takeover Provisions

Section 203 of the Delaware General Corporation Law. We are subject to Section 203 of the Delaware General Corporation Law, which prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years after the date that such stockholder became an interested stockholder, with the following exceptions:

- · before such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction began, excluding for purposes of determining the voting stock outstanding, but not the outstanding voting stock owned by the interested stockholder, those shares owned (i) by persons who are directors and also officers and (ii) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- on or after such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of the stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock that is not owned by the interested stockholder.

In general, Section 203 defines a "business combination" to include the following:

- · any merger or consolidation involving the corporation and the interested stockholder;
- $\cdot \quad \text{any sale, transfer, pledge or other disposition of } 10\% \text{ or more of the assets of the corporation involving the interested stockholder}; \\$
- · subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- · any transaction involving the corporation that has the effect of increasing the proportionate share of the stock or any class or series of the corporation beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits by or through the corporation.

In general, Section 203 defines an "interested stockholder" as an entity or person who, together with the person's affiliates and associates, beneficially owns, or within three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation.

Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws. Our amended and restated certificate of incorporation, or our restated certificate, provides for our board of directors to be divided into three classes with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. Because our stockholders do not have cumulative voting rights, stockholders holding a majority of the shares of common stock outstanding will be able to elect all of our directors. Our restated certificate and our amended and restated bylaws, or our restated bylaws, also provide that directors may be removed by the stockholders only for cause upon the vote of 66 2/3% or more of our outstanding common stock. Furthermore, the authorized number of directors may be changed only by resolution of the board of directors, and vacancies and newly created directorships on the

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Our restated certificate and restated bylaws also provide that all stockholder actions must be effected at a duly called meeting of stockholders and will eliminate the right of stockholders to act by written consent without a meeting. Our restated bylaws also provide that only our chairman of the board, chief executive officer or the board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors may call a special meeting of stockholders.

Our restated bylaws also provide that stockholders seeking to present proposals before a meeting of stockholders to nominate candidates for election as directors at a meeting of stockholders must provide timely advance notice in writing, and will specify requirements as to the form and content of a stockholder's notice.

Our restated certificate and restated bylaws provide that the stockholders cannot amend many of the provisions described above except by a vote of 66 2/3% or more of our outstanding common stock.

The combination of these provisions makes it more difficult for our existing stockholders to replace our board of directors as well as for another party to obtain control of us by replacing our board of directors. Since our board of directors has the power to retain and discharge our officers, these provisions could also make it more difficult for existing stockholders or another party to effect a change in management. In addition, the authorization of undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to effect a change of control of our company.

These provisions are intended to enhance the likelihood of continued stability in the composition of our board of directors and its policies and to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to reduce our vulnerability to hostile takeovers and to discourage certain tactics that may be used in proxy fights. However, such provisions could have the effect of discouraging others from making tender offers for our shares and may have the effect of delaying changes in our control or management. As a consequence, these provisions may also inhibit fluctuations in the market price of our stock that could result from actual or rumored takeover attempts. We believe that the benefits of these provisions, including increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure our company, outweigh the disadvantages of discouraging takeover proposals, because negotiation of takeover proposals could result in an improvement of their terms.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Continental Stock Transfer & Trust Company. The transfer agent's address is 17 Battery Place, 8th Floor, New York, NY 10004.

Listing on the Nasdaq Global Select Market

Our common stock is listed on the Nasdaq Global Select Market under the symbol "TRVN".

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PLAN OF DISTRIBUTION

We have entered into a Sales Agreement with Cowen under which we may issue and sell shares of our common stock having aggregate sales proceeds of up to \$75.0 million from time to time through Cowen acting as agent. Cowen may sell the common stock by any method that is deemed to be an "at-the-market" equity offering as defined in Rule 415 promulgated under the Securities Act including sales made directly on or through the Exchange or any other existing trading market for the common stock in the United States or to or through a market maker. Cowen also may sell the common stock in negotiated transactions, subject to our prior approval.

Each time we wish to issue and sell common stock under the sales agreement, we will notify Cowen of the number of shares to be issued, the dates on which such sales are anticipated to be made and any minimum price below which sales may not be made. Once we have so instructed Cowen, unless Cowen declines to accept the terms of this notice, Cowen has agreed to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. The obligations of Cowen under the sales agreement to sell our common stock are subject to a number of conditions that we must meet.

The settlement between us and Cowen is generally anticipated to occur on the third trading day following the date on which the sale was made. Sales of our common stock as contemplated in this prospectus will be settled through the facilities of The Depository Trust Company or by such other means as we and Cowen may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

We will pay Cowen a commission equal to an aggregate of up to 3% of the gross proceeds we receive from the sales of our common stock. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. In connection with the sale of the common stock on our behalf, Cowen may, and will with respect to sales effected in an "at-the-market-offering," be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation of Cowen will be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to Cowen with respect to certain civil liabilities, including liabilities under the Securities Act. In addition, we have agreed to reimburse Cowen for fees and disbursements related to its legal counsel in an amount not to exceed \$30,000, and for certain other expenses, including Cowen's FINRA counsel fees in an amount up to \$12,500. We estimate that the total expenses for the offering, excluding compensation payable to Cowen under the terms of the sales agreement, will be approximately \$300,000.

The offering of our common stock pursuant to the sales agreement will terminate upon the earlier of (i) the issuance and sale of all of our common stock provided for in this prospectus, or (ii) termination of the sales agreement as permitted therein.

This summary of the material provisions of the sales agreement does not purport to be a complete statement of its terms and conditions. A copy of the sales agreement is filed with the SEC and is incorporated by reference into the registration statement of which this prospectus is a part. See "Where You Can Find More Information" below.

To the extent required by Regulation M, Cowen will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus.

LEGAL MATTERS

The validity of the common stock offered by this prospectus will be passed upon by Cooley LLP, Washington, District of Columbia. Morgan, Lewis & Bockius, LLP, is counsel for Cowen in connection with this offering.

EXPERTS

The financial statements of Trevena, Inc. appearing in Trevena, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2014 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

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WHERE YOU CAN FIND MORE INFORMATION

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

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy the registration statement, as well as any other document filed by us with the SEC, at the SEC's Public Reference Room at 100 F Street NE, Washington, D.C. 20549. You can also request copies of these documents by writing to the SEC and paying a fee for the copying cost. You may obtain information on the operation of the Public Reference Room by calling the SEC at (800) SEC-0330. The SEC maintains a website that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including Trevena. The address of the SEC website is www.sec.gov.

We maintain a website at www.trevenainc.com. Information contained in or accessible through our website does not constitute a part of this prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The SEC file number for the documents incorporated by reference in this prospectus is 001-36193. The documents incorporated by reference into this prospectus contain important information that you should read about us.

The following documents are incorporated by reference into this document:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2014 filed with the SEC on March 18, 2015;
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2014 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed) filed with the SEC on April 3, 2015;
- · our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2015, June 30, 2015 and September 30, 2015 filed with the SEC on May 7, 2015, August 11, 2015 and November 10, 2015, respectively;
- · our Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on January 5, 2015, March 10, 2015, March 23, 2015, April 3, 2015, April 13, 2015, May 5, 2015, May 13, 2015, May 21, 2015, July 21, 2015, July 21, 2015, August 31, 2015, September 14, 2015, September 21, 2015, December 11, 2015 and December 14, 2015; and
- the description of our common stock, which is registered under Section 12 of the Exchange Act, in our registration statement on Form 8-A, filed with the SEC on November 12, 2013, including any amendments or reports filed for the purpose of updating such description.

We also incorporate by reference into this prospectus all documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (i) after the date of the initial filing of the registration statement of which this prospectus forms a part and prior to effectiveness of the registration statement, or (ii) after the date of this prospectus but prior to the termination of the offering. These documents

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include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as proxy statements.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, without charge upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits which are specifically incorporated by reference into such documents. You should direct any requests for documents by writing us at 1018 West 8th Avenue, Suite A, King of Prussia, PA 19406 Attn: Corporate Secretary or telephoning us at (610) 354-8840.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference into this document will be deemed to be modified or superseded for purposes of the document to the extent that a statement contained in this document or any other subsequently filed document that is deemed to be incorporated by reference into this document modifies or supersedes the statement.

DISCLOSURE OF COMMISSION'S POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITY

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling the Company pursuant to the foregoing provisions, we have been informed that in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable.

\$75,000,000



Common Stock

Prospectus

Cowen and Company

January 7, 2015