TREVENA INC
Form S-1
November 20, 2014

As filed with the Securities and Exchange Commission on November 20, 2014

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-1

REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

TREVENA, INC.

(Exact name of registrant as specified in its charter)

Delaware	**2834**	**26-1469215**
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

1018 West 8th Avenue, Suite A
King of Prussia, PA 19406
(610) 354-8840

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

John M. Limongelli, Esq.
Senior Vice President, General Counsel and Secretary
Trevena, Inc.
1018 West 8th Avenue, Suite A
King of Prussia, PA 19406
(610) 354-8840

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Brent B. Siler, Esq.
Derek O. Colla, Esq.
Cooley LLP
11951 Freedom Drive
Reston, Virginia 20190

Peter N. Handrinos, Esq.
Michael E. Sullivan, Esq.
Latham & Watkins LLP
John Hancock Tower
200 Clarendon Street

Telephone: (703) 456-8000
Fax: (703) 456-8100

Boston, MA 02116
Telephone: (617) 948-6000
Fax: (617) 948-6001

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

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

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

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 under the Securities Exchange Act of 1934. (Check one):

Large Accelerated Filer o	Accelerated Filer o	Non-accelerated Filer o (Do not check if a smaller reporting company)	Smaller Reporting Company ý

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	**Proposed Maximum Aggregate Offering Price(1)(2)**	**Amount of Registration Fee**
Common Stock, par value $0.001 per share	$46,000,000	$5,346

(1) Includes shares that the underwriters have the option to purchase.

(2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended.

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

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Subject to Completion, dated November 20, 2014

The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

PROSPECTUS

$40,000,000

Trevena, Inc.

Common Stock

This is an offering of $40,000,000 of shares of the common stock of Trevena, Inc. All of the shares of common stock are being sold by us.

Our common stock trades on the NASDAQ Global Select Market under the symbol "TRVN." On November 18, 2014, the last reported trading price of our stock was $5.87 per share.

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, have elected to comply with certain reduced public company reporting requirements.

Investing in our common stock involves risks. See "Risk Factors" beginning on page 14 of this prospectus.

	Per Share	Total
Price to the public	$	$
Underwriting discounts and commissions[1]	$	$
Proceeds to Trevena (before expenses)	$	$

[1] We refer you to "Underwriting" beginning on page 164 of this prospectus for additional information regarding underwriter compensation.

We have granted the underwriters the option to purchase up to $6,000,000 of additional shares of common stock on the same terms and conditions set forth above.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares on or about , 2014.

Barclays	Cowen and Company	Jefferies

JMP Securities	Needham & Company

Prospectus dated , 2014.

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We have not authorized anyone to provide any information or to make any representations other than those contained in this prospectus or in any free writing prospectuses we have prepared. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus is current only as of its date.

For investors outside the United States: We have not and the underwriters have not done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons who come into possession of this prospectus and any applicable free writing prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus and any such free writing prospectus applicable to that jurisdiction.

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PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our financial statements and the related notes thereto and the information set forth under the sections "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," in each case included in this prospectus. Unless the context otherwise requires, we use the terms "Trevena," "company," "we," "us" and "our" in this prospectus to refer to Trevena, Inc.

Company Overview

We are a clinical stage biopharmaceutical company that discovers, develops and intends to commercialize therapeutics that use a novel approach to target G protein coupled receptors, or GPCRs. Using our proprietary product platform, we have identified and advanced three differentiated product candidates into the clinic as follows:

TRV130: We recently announced top-line data from our Phase 2a/b clinical trial of TRV130 in postoperative pain. At doses of 2 mg and 3 mg of TRV130 administered every three hours, the trial achieved its primary endpoint of statistically greater pain reduction than placebo for 48 hours, which we believe demonstrates proof of concept for TRV130. The 3 mg dose of TRV130 also showed statistically superior analgesic efficacy over the 48-hour trial period compared to 4 mg of morphine administered every four hours. Additionally, in the first three hours of dosing, when pain was most severe, the 1 mg, 2 mg and 3 mg doses of TRV130 demonstrated superior analgesic efficacy in the trial compared to placebo, and the 2 mg and 3 mg doses of TRV130 demonstrated superior analgesic efficacy compared to 4 mg of morphine. There were no serious adverse events reported in the trial, which we believe suggests that these levels of pain relief can be achieved safely. Over the 48-hour trial period, the tolerability of TRV130 at doses of 2 mg and 3 mg administered every three hours was similar to that of 4 mg of morphine administered every four hours. Based on these data, we plan to move into Phase 3 preparations, which we expect to occur in parallel with a second Phase 2 trial we are planning for TRV130. These data complement the data generated in our Phase 1b trial, in which TRV130 showed superior efficacy with an improved tolerability profile following a single dose of TRV130 relative to a 10 mg dose of morphine in a human evoked-pain model. We hold a U.S. patent covering the composition of matter and methods of use for TRV130. We have retained all worldwide development and commercialization rights to TRV130, and plan to commercialize it in acute care markets such as hospitals and ambulatory surgery centers if it receives regulatory approval.

TRV734: We have completed a first Phase 1 single ascending dose clinical trial for TRV734, an oral follow-on to TRV130 for the treatment of moderate to severe acute and chronic pain. We have completed enrollment in a second Phase 1 multiple ascending dose clinical trial and expect to report data from this trial early in the first quarter of 2015. We have retained all worldwide development and commercialization rights to TRV734.

TRV027: We have completed a Phase 2a clinical trial and in early 2014 we initiated a Phase 2b clinical trial of TRV027 for acute heart failure, or AHF. Enrollment in this trial is ongoing, with over 200 patients recruited out of planned enrollment of approximately 500 patients. More than 65 sites in 12 countries are now open and recruiting, and we expect patient enrollment will conclude in the third quarter of 2015. We expect to report top-line data from this trial in the fourth quarter of 2015. Actavis plc, or Actavis, has the exclusive option to license TRV027 from us. We plan for TRV027 to be commercialized in the acute care hospital market if it receives regulatory approval.

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We also plan to identify a product candidate from our preclinical δ-opioid receptor program focused on central nervous system, or CNS, indications in 2014 and to advance the product candidate to preclinical studies in 2015 that would support our submission of an investigational new drug application, or IND, to the U.S. Food and Drug Administration, or FDA.

Our Pipeline

Our Platform

GPCRs are a large family of cell surface receptors that trigger two signaling pathways, G protein and β-arrestin, and are implicated in cellular function and disease processes. More than 30% of all currently marketed therapeutics target GPCRs. Currently available therapeutics that target GPCRs, or GPCR ligands, are typically not signal specific, and therefore either inhibit both the G protein and β-arrestin pathways (an antagonist ligand) or activate both pathways (an agonist ligand). This lack of signal specificity often results in a suboptimal therapeutic profile for these drugs because in many cases one of the pathways is associated with a beneficial therapeutic effect and the other is associated with limiting that benefit or with an undesirable side effect (see Figure 1). We use our proprietary Advanced Biased Ligand Explorer, or ABLE, product platform to identify "biased" ligands, which are compounds that activate one of the two signaling pathways of the GPCR while inhibiting the other (see Figure 2). This signaling specificity is the basis for our drug discovery and development approach, which is to identify selective GPCR biased ligands and develop them into differentiated clinical products. While some GPCRs trigger other signaling pathways in addition to G protein and β-arrestin, most GPCRs trigger those two pathways.

Our ABLE product platform is a collection of proprietary biological information, *in vitro* assays, know-how and expertise that we use to identify unique GPCR-targeted biased ligands with attractive pharmaceutical properties. Our *in vitro* assays use cells that have the receptor of interest on the cell surface, where G protein and β-arrestin signaling from that receptor can be measured to determine if a

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particular ligand is biased, and if so whether it is a G protein or β-arrestin biased ligand. Our assays can also measure different cellular responses resulting from signaling through β-arrestin and can thereby help us to associate pharmacological responses with molecular signaling. Most components of our ABLE product platform are maintained as trade secrets, but the output of the product platform is reflected in the product candidates that we have advanced into clinical testing and the research we have published in numerous peer-reviewed journals. We believe that our ABLE product platform provides us with an important competitive advantage in identifying further opportunities for efficient and high-impact biased ligand drug discovery, development and commercialization.

We were founded in late 2007 to discover and develop product candidates based on biased ligands, a concept discovered by our scientific founder, Dr. Robert Lefkowitz, who was awarded the 2012 Nobel Prize in Chemistry in part for his elucidation of the multiple pathways that a GPCR engages. We believe that we are the first company to progress a GPCR biased ligand into clinical trials. The members of our executive management team have held senior positions at leading pharmaceutical and biotechnology companies and possess substantial experience across the spectrum of drug discovery, development and commercialization.

Figure 1: Mechanism of current GPCR-targeted drugs

Figure 2: Mechanism of our biased ligands the next generation of GPCR-targeted drugs

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CNS Portfolio

TRV130

TRV130 is a small molecule G protein biased ligand at the μ-opioid receptor that we are developing as a first-line treatment for patients experiencing moderate to severe acute pain where intravenous, or IV, administration is preferred. The μ-opioid receptor is a well-established target for analgesics such as fentanyl and morphine, which are unbiased μ-opioid agonists. TRV130 activates the μ-opioid G protein pathway, associated with analgesia, and inhibits the β-arrestin pathway, which, in preclinical studies, was associated with limiting opioid analgesia, and with promoting opioid-induced respiratory depression and constipation. We believe that the management of moderate to severe, acute postoperative pain represents the largest opportunity for an intravenously administered μ-opioid therapy like TRV130. Accordingly, we have focused our initial clinical trials on the treatment of surgical patients. We believe that delivering better pain relief or mitigating dose limiting side effects typically associated with the activation of the μ-opioid receptor will position TRV130, if approved, to more effectively treat postoperative pain than currently available μ-opioid therapies.

According to data from IMS Health, a healthcare information firm, in 2013 there were approximately 47 million hospital inpatient stays and outpatient visits during which reimbursement claims for injectable opioids were made, 20 million of which involved a surgical procedure. Given its pharmacokinetic, tolerability and efficacy profile in our Phase 1 and Phase 2a/b clinical trials, we believe that both the inpatient and outpatient settings could be appropriate for TRV130 use. Despite the adoption of postoperative pain management guidelines, significant unmet need remains. In a 2012 survey of 300 surgical patients in the United States, over 80% of patients reported postoperative pain after the first analgesic medication had been administered, and 40% of those patients reported this pain to be moderate or severe. Currently available μ-opioid agonists, such as morphine and fentanyl, are the most effective class of analgesics for moderate to severe acute postoperative pain, but their effectiveness is limited in part because their doses are limited by severe side effects such as respiratory depression, nausea and vomiting, constipation and postoperative ileus, which is a condition that most commonly occurs after surgery involving interruption of movement of the intestines in which the bowel enters spasm and stops passing food and waste.

We have announced top-line data from our Phase 2a/b clinical trial of TRV130 in postoperative pain. At doses of 2 mg and 3 mg of TRV130 administered every three hours, the trial achieved its primary endpoint of statistically greater pain reduction than placebo for 48 hours, which we believe demonstrates proof of concept for TRV130. The 3 mg dose of TRV130 also showed statistically superior analgesic efficacy over the 48-hour trial period compared to 4 mg of morphine administered every four hours. Additionally, in the first three hours of dosing, when pain was most severe, the l mg, 2 mg and 3 mg doses of TRV130 demonstrated superior analgesic efficacy in the trial compared to placebo, and the 2 mg and 3 mg doses of TRV130 demonstrated superior analgesic efficacy compared to 4 mg of morphine. There were no serious adverse events reported in the trial, which we believe suggests that these levels of pain relief can be achieved safely. Over the 48-hour trial period, the tolerability of TRV130 at doses of 2 mg and 3 mg administered every three hours was similar to that of 4 mg of morphine administered every four hours. Based on these data, we plan to move into Phase 3 preparations, which we expect to occur in parallel with a second Phase 2 trial we are conducting for TRV130.

In our Phase 1b clinical trial in healthy subjects using an evoked-pain model, TRV130 showed superior analgesia compared to a high dose of morphine following a single dose administration, while causing less respiratory depression, less severe nausea and less vomiting. Together with our top-line Phase 2a/b data, we believe these results suggest that TRV130 may have an improved clinical profile in terms of efficacy, safety and tolerability compared to unbiased μ-opioid agonists, which are the current standard of care.

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We plan to initiate a second Phase 2 clinical trial in the fourth quarter of 2014 in soft tissue pain to inform Phase 3 development, since efficacy in both hard and soft tissue pain would be required by the FDA for a broad label in the treatment of acute moderate to severe pain. This trial will use flexible, as-needed dosing to allow patients to control the balance of efficacy and tolerability as their needs change over time. We expect to report top-line data from this second Phase 2 clinical trial in mid-2015. Prior to later-phase clinical development, we are also conducting or planning additional Phase 1 clinical testing in healthy subjects to add to our clinical understanding of TRV130.

We intend to retain full commercialization rights in the United States for TRV130. After the availability of the final Phase 2a/b clinical data for TRV130, we may seek collaborators for commercializing TRV130 outside of the United States to offset risk and preserve capital. We may also seek to collaborate with a third party to evaluate novel formulations of TRV130 for chronic pain and breakthrough pain. We have an issued U.S. patent that covers TRV130, compositions comprising TRV130 and methods of using TRV130, and this patent is expected to expire no earlier than 2032.

TRV734

TRV734 is a small molecule G protein biased ligand targeting the μ-opioid receptor, which we are developing as a first-line, orally administered compound for the treatment of moderate to severe acute and chronic pain. Like TRV130, TRV734 takes advantage of a well-established mechanism of pain relief by targeting the μ-opioid receptor, but does so with enhanced selectivity for the G protein signaling pathway, which in preclinical studies was linked to analgesia, as opposed to the β-arrestin signaling pathway, which in preclinical studies was associated with limiting analgesic efficacy and with promoting opioid-induced respiratory depression and constipation. Subject to successful non-clinical and clinical development and regulatory approval, we believe TRV734 may have an improved profile of efficacy relative to tolerability, or therapeutic profile, as compared to current commonly prescribed oral analgesics, such as oxycodone. We have filed patent applications covering TRV734 and methods of using TRV734.

In a Phase 1 single ascending dose clinical trial in healthy subjects, using pupil constriction as a surrogate for the analgesic efficacy of opioid drugs, orally administered TRV734 showed pharmacokinetics and pharmacodynamics across a dose range that was generally safe and well tolerated. These data supported further development, and we have completed enrollment in a second Phase 1 clinical trial, which is a multiple ascending dose trial evaluating the safety, tolerability, pharmacodynamics and pharmacokinetics of TRV734 given as a single dose and as multiple ascending doses in healthy volunteers. The aim of this trial is to support Phase 2 development, and top line data are expected early in the first quarter of 2015. We intend to seek a collaborator with experience in developing and commercializing controlled-substance therapeutics in acute and chronic care pain markets, thereby leveraging their expertise while retaining rights to commercialize TRV734 in treatment settings for which we can leverage our commercial strategy for TRV130.

δ-opioid receptor program

We are pursuing a research program to identify a small molecule G protein biased ligand targeting the δ-opioid receptor for the treatment of CNS disorders, which may include migraine, Parkinson's disease or neuropathic pain. We expect to identify a product candidate by the end of 2014. We intend to seek a collaborator with CNS experience to leverage their expertise in development and commercialization of a δ-opioid receptor product candidate, retaining rights for any acute care indications in the United States.

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Cardiovascular Program

TRV027

We are developing TRV027 as a first-line IV treatment in combination with standard diuretic therapy for AHF patients. TRV027 is a peptide β-arrestin biased ligand that targets the angiotensin II type 1 receptor, or AT1R, which is a GPCR expressed on cells in the cardiovascular system. TRV027 inhibits G protein signaling and activates β-arrestin signaling. In our Phase 2a clinical trial, TRV027 rapidly reduced blood pressure and preserved renal, or kidney, function, while preserving cardiac performance. We are enrolling patients in a Phase 2b clinical trial to evaluate the safety and efficacy of TRV027 in AHF. Over 200 patients have been recruited out of planned enrollment of approximately 500 patients. More than 65 sites in 12 countries are open and recruiting, and we expect patient enrollment to conclude in the third quarter of 2015. We expect to report data from this trial by the end of the fourth quarter of 2015. If subsequent Phase 3 development is successful and TRV027 is approved by regulatory authorities, we believe TRV027 would be used as a first-line in-hospital AHF treatment. We also believe TRV027 could improve AHF symptoms, shorten length of hospital stay in the short term, and potentially lower readmission rates and mortality rates in the long term.

There are over 20 million people living with heart failure in the United States and Europe, according to the American Heart Association and the European Society of Cardiology. AHF, also sometimes referred to as acute decompensated heart failure, is heart failure requiring hospitalization. AHF patients present with severe dyspnea, a serious shortness of breath sometimes described as "air hunger," and fluid overload, leading to an inability to perform simple functions such as standing and walking short distances. This can also lead to organ dysfunction, including dysfunction in the kidneys and heart. The National Hospital Discharge Survey reported over five million hospital discharges in the United States in 2010 where heart failure was listed as a component of the diagnosis, over one million of which listed heart failure as the primary diagnosis. TRV027 has shown beneficial effects on the three key organ systems affected in heart failure, the blood vessels, heart and kidneys in our preclinical studies and Phase 1b and 2a clinical trials. In combination with standard diuretics, we believe these effects may translate into improvements in symptoms and outcomes such as hospital readmission rates, length of hospital stay and mortality rates if TRV027 successfully completes Phase 3 development and is approved by regulatory authorities.

Safety and tolerability issues limit the effectiveness of currently available AHF treatments. We believe that TRV027's tolerability profile differentiates it from current therapies. In healthy subjects in our Phase 1 clinical trial, there were no serious adverse events, even at doses 20 times higher than the expected therapeutic dose. In addition, there were no TRV027-related serious adverse events in a Phase 2a clinical trial in medically fragile, advanced chronic heart failure subjects and no clinically significant adverse events in subjects with heart failure and concomitant renal impairment. Finally, in preclinical toxicology studies, TRV027 had a favorable profile at doses up to 500 times the expected therapeutic dose.

In May 2013, we entered into an option agreement and a license agreement with Forest Laboratories Holdings Limited, or Forest, under which we granted to Forest an exclusive option to license TRV027, which may be exercised at any time before we deliver our Phase 2b clinical trial results to Forest and during a specified period of time thereafter. In July 2014, Actavis plc, or Actavis, acquired Forest, including Forest's option to TRV027. If Actavis exercises its option, the license agreement between us and Actavis will become effective, and Actavis will have an exclusive worldwide license to develop and commercialize TRV027 and specified related compounds. Actavis will be responsible for subsequent development, regulatory approval and commercialization of TRV027 at Actavis's expense. If Actavis exercises the option, we would receive a $65 million option exercise fee and could potentially receive up to $365 million depending upon the achievement of future development and commercial milestones. We could also receive tiered royalties between 10% and 20%

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on net sales of licensed products worldwide, with the royalty rates on net sales of licensed products in the United States being somewhat higher than the royalty rates on net sales of licensed products outside the United States. We have three issued U.S. patents covering the composition of matter and method of use of TRV027 that are expected to expire no earlier than 2031 and 2029, respectively.

Our Strategy

Our goal is to build a leading biopharmaceutical company leveraging our expertise in biased ligands to develop and commercialize innovative, best-in-class drugs targeting established GPCRs. Key elements of our business strategy to achieve this goal are to:

- rapidly advance development of our three clinical-stage product candidates, TRV130, TRV734 and TRV027, to commercialization;
- establish commercialization and marketing capabilities in the United States, initially in acute care markets, for any of our product candidates that are approved or that we anticipate may be approved;
- expand our CNS product portfolio by advancing our preclinical δ-opioid receptor program; and
- leverage our ABLE product platform to continue to discover innovative biased ligand therapeutics and expand our product platform's impact through external collaborations.

Financial Overview

Our revenue to date has been generated primarily through research grants and a research collaboration. We have not generated any commercial product revenue. As of September 30, 2014, we had $72.2 million of cash and cash equivalents and an accumulated deficit of $118.7 million.

In September 2014, we announced we had entered into a $35.0 million senior secured tranched term loan credit facility with Oxford Finance LLC and Square 1 Bank, of which we have drawn $2.0 million as of the date of this prospectus. The facility also provides for up to two additional term loan tranches of $16.5 million each. Based on the top-line results of the Phase 2a/b clinical trial of TRV130 announced in November 2014, we believe we have met the conditions to draw the second tranche of $16.5 million tranche from the credit facility. We may opt to draw the third term loan tranche if we receive positive data from the Phase 2 clinical trial of TRV027.

We believe that existing cash and the available borrowings under the second tranche of our credit facility, excluding any potential future draw from our credit facility if we receive positive data from the Phase 2 study of TRV027, plus the net proceeds from the offering will be sufficient to fund our operations through the end of 2016.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the "Risk Factors" section of this prospectus. These risks include the following:

- We will need substantial additional funding to pursue our business objectives. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our drug development programs or potential commercialization efforts.
- We are early in our development efforts and have only two product candidates, TRV027 and TRV130, in Phase 2, and one more, TRV734, in Phase 1. If we, or Actavis if it exercises its option to license TRV027, are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

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Our preclinical δ-opioid receptor program may not successfully identify a product candidate.

If Actavis exercises its option to license TRV027, that relationship will be significant to our business. If Actavis' development and commercialization of TRV027 is not successful, our business could be adversely affected.

We have incurred significant losses since our inception. We expect to continue to incur losses over the next several years and may never achieve or maintain profitability.

We face substantial competition, which may result in others discovering, developing or commercializing drugs before or more successfully than we do.

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

Corporate Information

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.

Implications of Being an Emerging Growth Company

As a company with less than $1 billion in revenue during our last fiscal year, we qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from specified 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 our 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 nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We may take advantage of these provisions through 2019 or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than $1 billion in annual revenue, have more than $700 million in market value of our capital stock held by non-affiliates or issue more than $1 billion of non-convertible debt over a three-year

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period. We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of some reduced reporting burdens in this prospectus. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

In addition, 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 provision allows an emerging growth company to delay the adoption of some accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

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The Offering

Common stock offered by Trevena	$40,000,000 of shares of common stock.
Total common stock to be outstanding after this offering	shares (shares if the underwriters elect to exercise their option to purchase additional shares from us in full).
Option to purchase additional shares of common stock	The underwriters have an option to purchase a maximum of $6,000,000 of additional shares from us. The underwriters can exercise this option at any time within 30 days from the date of this prospectus.
Use of proceeds	We expect the net proceeds to us from this offering, after expenses, to be approximately $ million, or approximately $ million if the underwriters exercise their option to purchase additional shares from us in full. We intend to use the net proceeds from this offering as follows: to fund approximately $30.0 million of clinical development expenses, including for our ongoing Phase 2b clinical trial of TRV027, our completion of Phase 2 and initiation of Phase 3 clinical trials for TRV130 and the conduct of development activities for TRV734; and the remaining proceeds will be used for preclinical research and development efforts and for working capital and general corporate purposes. See "Use of Proceeds" on page 51 for additional information.
Risk factors	See the section titled "Risk Factors" beginning on page 14 and the other information included in this prospectus for a discussion of factors you should carefully consider before deciding to invest in our common stock.
NASDAQ Global Select Market symbol	TRVN

The number of shares of our common stock that will be outstanding after this offering is based on 26,376,626 shares of common stock outstanding as of September 30, 2014 and assumes the sale of $40,000,000 of shares of common stock at an assumed public offering price of $ per share, which was the last reported sale price of our common stock on the NASDAQ Global Select Market on , 2014. A 5% increase or decrease in the assumed public offering price of $ per share would decrease or increase the number of shares of our common stock issued in this offering by approximately 5%.

The number of shares of our common stock that will be outstanding after this offering set forth above excludes:

- 3,552,124 shares of our common stock issuable upon the exercise of stock options outstanding under our 2008 Equity Incentive Plan and 2013 Equity Incentive Plan as of September 30, 2014, at a weighted average exercise price of $3.72 per share;

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30,258 shares of our common stock issuable upon exercise of warrants outstanding as of September 30, 2014, at a weighted average exercise price of $5.62 per share;

33,000 shares of our common stock issuable upon the exercise of stock options granted after September 30, 2014, at a weighted average exercise price of $5.18 per share; and

868,235 shares of our common stock reserved for future issuance as of September 30, 2014 under our 2013 Equity Incentive Plan and our employee stock purchase plan.

Except as otherwise indicated herein, all information in this prospectus, including the number of shares that will be outstanding after this offering, assumes or gives effect to:

no exercise of options or warrants outstanding as of September 30, 2014; and

no exercise of the underwriters' option to purchase additional shares in this offering.

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Summary Financial Data

The following tables set forth our summary financial data for the periods indicated. The following summary financial data for the years ended December 31, 2012 and 2013 are derived from our audited financial statements, which have been audited by Ernst & Young LLP, our independent registered public accounting firm, appearing elsewhere in this prospectus. We have derived the following summary of our statement of operations data for the nine months ended September 30, 2013 and 2014 and the balance sheet data as of September 30, 2014 from our unaudited condensed financial statements appearing elsewhere in this prospectus.

The financial data for the nine months ended September 30, 2013 and 2014 and as of September 30, 2014 includes, in the opinion of our management, all adjustments, consisting only of normal recurring adjustments that are necessary for a fair presentation of our financial position and results of operations for these periods. Our historical results are not necessarily indicative of the results to be expected in the future, and our operating results for the nine months ended September 30, 2014 are not necessarily indicative of the results that may be expected for the entire year ending December 31, 2014.

This summary financial data should be read together with the historical financial statements and related notes to those statements, as well as "Management's Discussion and Analysis of Financial Condition and Results of Operations," which are included elsewhere in this prospectus.

	Year Ended December 31,		Nine Months Ended September 30,	
	2012	2013	2013	2014
	(in thousands, except share and per share data)			
Statement of Operations Data:				
Total revenue	$ 808	$ 135	$ 135	$
Operating expenses:				
General and administrative	3,123	4,718	2,843	7,034
Research and development	13,295	18,762	12,240	29,671
Total operating expenses	16,418	23,480	15,083	36,705
Loss from operations	(15,610)	(23,345)	(14,948)	(36,705)
Total other income (expense)	(26)	94	(1,398)	301
Net loss and comprehensive loss	(15,636)	(23,251)	(16,346)	(36,404)
Accretion of redeemable convertible preferred stock	(316)	(334)	(248)	(28)
Net loss attributable to common stockholders	$ (15,952)	$ (23,585)	$ (16,594)	$ (36,432)