Confidential Draft No. 2 submitted to the Securities and Exchange Commission on September 29, 2014.

Registration No. 333-

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM S-1

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

INOTEK PHARMACEUTICALS CORPORATION

(Exact Name of Registrant as Specified in Its Charter)

Delaware	2834	04-3475813
(State or Other Jurisdiction of Incorporation or Organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

131 Hartwell Avenue, Suite 105
Lexington, MA 02421
(781) 676-2100
(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

David P. Southwell
President and Chief Executive Officer
131 Hartwell Avenue, Suite 105
Lexington, MA 02421
(781) 676-2100
(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent For Service)

Copies to:

Mitchell S. Bloom **Edwin M. O'Connor** **Goodwin Procter LLP** **Exchange Place** **53 State Street** **Boston, MA 02109** **(617) 570-1000**	**Mark B. Weeks** **Babak Yaghmaie** **Divakar Gupta** **Cooley LLP** **1114 Avenue of the Americas** **New York, NY 10036** **(212) 479-6000**

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, as amended, check the following box. ☐

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

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. ☐

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

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

Large Accelerated Filer ☐	Accelerated Filer ☐
Non-Accelerated Filer (Do not check if a smaller reporting company) ☒	Smaller Reporting Company ☐

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 $0.01 per share	**$**	**$**

(1) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act.
(2) Includes the offering price of shares that the underwriters have the option to purchase to cover over-allotments, if any.

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

Table of Contents

PROSPECTUS (Subject to completion) **Dated , 2014**

Shares

Common Stock

This is an initial public offering of shares of our common stock. We are offering shares of our common stock. Prior to this offering, there has been no public market for our common stock. We intend to apply to list our common stock on The NASDAQ Global Market under the symbol "ITEK." We expect that the initial public offering price of our common stock will be between $ and $ per share.

We are an "emerging growth company" under applicable Securities and Exchange Commission rules and will be subject to reduced public company reporting requirements for this prospectus and future filings. See "Prospectus Summary—Implications of Being an Emerging Growth Company."

Our business and an investment in our common stock involve significant risks. These risks are described under the caption "Risk Factors" beginning on page 12 of this prospectus.

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

	Per Share	*Total*
Initial public offering price	**$**	**$**
Underwriting discounts and commissions(1)	**$**	**$**
Proceeds, before expenses, to Inotek	**$**	**$**

(1) We refer you to "Underwriting" beginning on page 151 for additional information regarding total underwriting compensation.

The underwriters may also purchase up to an additional shares from us at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus to cover overallotments.

The underwriters expect to deliver the shares against payment in New York, New York on , 2014.

Cowen and Company **Piper Jaffray**

, 2014

TABLE OF CONTENTS

You should rely only on the information contained in this prospectus or in any free writing prospectus prepared by us or on our behalf. We have not, and the underwriters have not, authorized any other person 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 underwriters are 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 is accurate only as of the date on the front cover of this prospectus. Our business, financial condition, results of operations and prospects may have changed since that date.

Information contained on our website is not part of this prospectus. Neither we nor any of the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. You are required to inform yourself about, and to observe any restrictions relating to, this offering and the distribution of this prospectus.

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 included elsewhere in this prospectus. You should also consider, among other things, the matters described under "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," in each case appearing elsewhere in this prospectus. Unless otherwise stated, all references to "us," "our," "Inotek," "we," the "Company" and similar designations refer to Inotek Pharmaceuticals Corporation.

Overview

We are a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of therapies for glaucoma. Glaucoma is a disease of the eye that is typically characterized by structural evidence of optic nerve damage, vision loss and consistently elevated intraocular pressure, or IOP. Our lead product candidate, *trabodenoson*, is a first-in-class selective adenosine mimetic that we rationally designed to lower IOP by restoring the eye's natural pressure control mechanism. We developed this molecule to selectively stimulate a particular adenosine subreceptor in the eye with the effect of augmenting the intrinsic function of the eye's trabecular meshwork, or TM. The TM regulates the pressure inside the eye, and is also the main outflow path for the fluid inside of the eye that often builds up pressure in patients with glaucoma. We believe that by restoring the natural function of the TM and this outflow path, rather than changing the fundamental dynamics of pressure regulation in the eye, *trabodenoson*'s mechanism of action should result in a lower risk of unintended side effects and long term safety issues than other mechanisms of action. Additionally, *trabodenoson*'s unique mechanism of action in the TM should complement the activity of existing glaucoma therapies that exert their IOP-lowering effects on different parts of the in-flow and out-flow system of the eye.

Our product pipeline includes *trabodenoson* monotherapy delivered in an eye drop formulation, as well as a fixed-dose combination, or FDC, of *trabodenoson* with *latanoprost* given once-daily, or QD. Statistically significant results for the primary endpoint of our completed Phase 2 clinical trial indicate that *trabodenoson* monotherapy has IOP-lowering effects in line with the best existing therapies, with a favorable safety and tolerability profile at all doses tested.

We are completing a Phase 2 trial of *trabodenoson* with *latanoprost* and expect results from this trial to be reported in the fourth quarter of 2014. We are planning an End-of-Phase 2 meeting with the U.S. Food and Drug Administration, or FDA, for *trabodenoson* monotherapy in the first half of 2015. We expect to initiate a Phase 3 program for *trabodenoson* monotherapy in mid-2015, which will consist of two Phase 3 pivotal trials and a long-term safety study. Based on our estimates of the rate of patient enrollment and assuming commencement in mid-2015, we expect to report top-line data from the first of the two pivotal Phase 3 trials by late 2016 or early 2017, with a second pivotal trial being completed in 2017. If the primary objectives of our Phase 3 program are met, we plan to submit a New Drug Application, or NDA, to the FDA for marketing approval of *trabodenoson* for the treatment of glaucoma in the United States. We plan to submit a marketing authorization application, or MAA, in Europe after filing our NDA for approval of *trabodenoson* in the United States.

We own worldwide rights to all indications for our current product candidates and have patents and pending patent applications related to the composition of matter, pharmaceutical compositions and methods of use for *trabodenoson*, certain of which extend to 2031 with respect to our issued patents and 2034 with respect to our pending patent applications, if issued. If *trabodenoson* receives marketing approval in the United States, we plan to commercialize it by establishing our own specialty sales force in the United States.

Glaucoma Market

According to IMS Health, sales of glaucoma drugs in 2013 were approximately $2.0 billion in the United States and $5.6 billion worldwide. According to the British Journal of Ophthalmology, there were an estimated 2.8 million Americans with glaucoma in 2010. Once glaucoma develops, it is a chronic condition that requires life-long treatment. Prostaglandin analogs, or PGAs, are the most widely prescribed drug class for glaucoma and include the most widely prescribed glaucoma drug, *latanoprost.* When PGA monotherapy is insufficient to control IOP or is poorly tolerated, non-PGA products, such as beta blockers, alpha agonists and carbonic anhydrase inhibitors, are generally used either as an add-on therapies to the PGA or as an alternative monotherapy. Both PGAs and non-PGAs can cause adverse effects in the eye. In addition, non-PGA drugs can have adverse effects in the rest of the body and have been shown to have poor tolerability profiles.

Additionally, no existing treatments offer the potential to directly treat the underlying cause of glaucoma associated vision loss: the death of retinal ganglion cells, or RGCs, which comprise the nerve tissue in the retina that relays the visual signal to the brain. We believe that a drug with the potential to make these cells more resilient to the stress caused by glaucoma would achieve broad market acceptance as the treatment preferred among patients and physicians.

We believe there are currently two leading classes of new drugs in clinical development for glaucoma: Rho kinase inhibitors and adenosine mimetics. Certain Rho kinase inhibitors recently entered Phase 3 clinical trials and are the furthest along of the potential new glaucoma therapies. Like with PGAs, eye redness, or conjunctival hyperemia, has been reported with the Rho kinase inhibitor class. Adenosine mimetics are compounds that mimic or simulate some of the actions or effects of adenosine, a naturally-occurring molecule with many, diverse biologic effects. We believe we are the only company to be developing an adenosine mimetic highly selective for the A1 subreceptor for ophthalmic indications.

Since 1996, there have been no new drug classes approved in the United States for glaucoma. As a result, there are persistent inadequacies in the tools that ophthalmologists use to manage patients with glaucoma. Thus, we believe there is a need for an innovative glaucoma treatment that offers:

- significant IOP-lowering;
- a favorable safety and tolerability profile;
- a novel mechanism of action that complements existing therapies; and
- convenient dosing.

Our Solution—*Trabodenoson*

Trabodenoson is a first-in-class selective adenosine mimetic that is designed to lower IOP with a mechanism of action that we believe augments the natural function of the TM. In addition, by enhancing a naturally occurring process to make the eye function more like that of a younger,

healthier eye, rather than changing the fundamental dynamics of pressure regulation in the eye, we believe there is a lower risk of unintended side effects that could result in safety or tolerability issues in the long term. We believe *trabodenoson* enhances metabolic activity in the TM, which helps clear the pathway for fluid in the eye, called aqueous humor, to flow out of the eye, thereby lowering IOP. We believe that *trabodenoson*'s mechanism of action improves the function of the eye, and that *trabodenoson* has the potential to be used as a monotherapy in place of current glaucoma treatments. In addition, we expect that *trabodenoson*'s purported mechanism of action in the TM should complement the activity of all currently-approved glaucoma drugs that work in other ways to lower IOP.

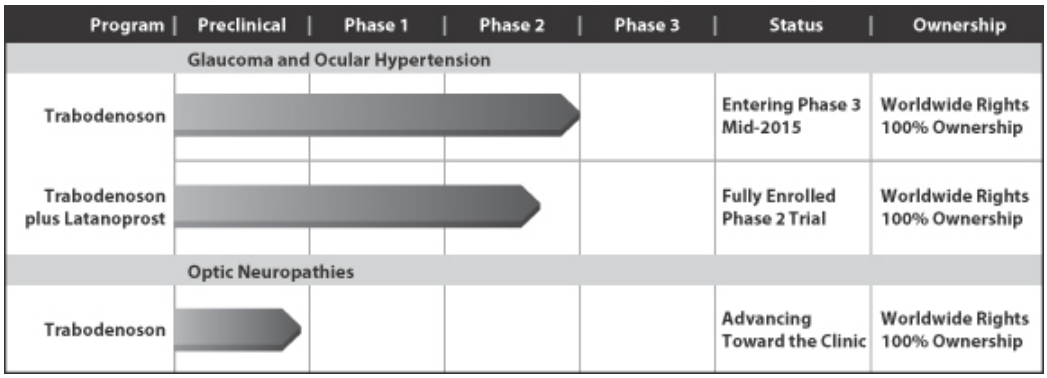
We believe the following elements of *trabodenoson*'s product profile will drive its adoption, if approved, in the glaucoma market:

- **Meaningful IOP-Lowering.** After four weeks of treatment in a Phase 2 clinical trial in glaucoma patients, *trabodenoson* (500 mcg) lowered IOP by an average of 6.5 mmHg from baseline. Moreover, IOP-lowering at week four was significantly better than IOP-lowering at week two. IOP-lowering for currently-approved glaucoma therapies, according to their FDA-approved labeling, ranges from 2-8 mmHg.
- **Favorable Safety Profile.** In three completed *trabodenoson* clinical trials over a wide range of doses, no patients have been withdrawn due to a *trabodenoson*-related side effect in the eye. In our most recently completed multiple-dose Phase 2 clinical trial, we did not observe side effects in the eye that would indicate a tolerability problem at any of the doses tested. Specifically, there was no change in the background rate of conjunctival hyperemia in the patient population when treatment with *trabodenoson* was initiated or continued for up to 28 days, even at the highest dose tested. No systemic effects of the drug have been identified despite rigorous monitoring, including cardiac and renal function, when administered as an eye drop. We believe this safety profile could be important in the potential for *trabodenoson* to become a preferred treatment alternative for patients that experience undesired side effects with existing therapies.
- **Unique, Complementary Mechanism of Action.** We believe that *trabodenoson*'s mechanism of action augments a naturally occurring process by clearing the path for aqueous humor outflow in the TM. We expect that this mechanism of action should complement all currently-approved glaucoma drugs which work in other ways to lower IOP, including by reducing the aqueous humor production or increasing outflow through the uveoscleral pathway. This makes *trabodenoson*, with its favorable safety profile, a candidate to add to other glaucoma medications when a further reduction of the IOP is desirable.
- **Convenient Dosing.** Current clinical data indicate that twice-a-day, or BID, dosing with *trabodenoson* is well tolerated and lowers IOP significantly. Moreover, after 28 days of BID dosing, the IOP-lowering effect persisted for an additional 24 hours after the last dose of medication, which suggests that *trabodenoson* could be dosed QD. We believe a QD dosing regimen minimizes the burden on patients to remember to take their medication, thus potentially improving compliance with the therapy. If confirmed in our Phase 3 program, BID or QD dosing would make *trabodenoson* easier to use than most non-PGA products, and if QD dosing is confirmed and approved, *trabodenoson*'s dosing frequency would match the best-in-class PGAs and would also facilitate an FDC that could be dosed once a day.

We believe that *trabodenoson*'s efficacy, complementary mechanism of action, dosing profile and safety profile also make it well-suited for use in an FDC with a PGA, which could be an effective and convenient option for patients currently using two or more glaucoma drugs to lower IOP.

Product Pipeline

Our product pipeline includes *trabodenoson*, as a monotherapy delivered in an eye drop formulation, as well as an FDC that includes *trabodenoson* plus *latanoprost* in an eye drop formulation. We are also evaluating the potential for *trabodenoson* to directly target optic nerve neuropathies. The following table summarizes key information about our product development programs.



Trabodenoson

Our first product candidate, *trabodenoson*, is a monotherapy dosed in an eye drop. Our clinical trials have shown that *trabodenoson* has significant IOP-lowering effects, convenient dosing and also has a favorable safety profile when compared to the currently available glaucoma treatments, such as PGAs and non-PGAs.

Trabodenoson-Latanoprost Fixed-Dose Combination

A large number of patients use more than one drug in an attempt to lower IOP. The available FDC products increase IOP-lowering but also have unpleasant tolerability challenges in the eye, as well as the adverse effects, safety warnings, precautions and contraindications that the two individually-dosed drugs carry in their FDA-approved package inserts. An FDC product containing a PGA plus a non-PGA has not yet been approved in the United States. We believe that none have gained FDA approval because the modest incremental benefit in IOP-lowering seen when a non-PGA is added to a PGA is too small in the context of the added side effects and clinical risks that come with the combined drugs. In contrast, we believe that an FDC containing a PGA and *trabodenoson* will benefit from significant incremental efficacy while adding very few side effects or clinical risks to the profile of the PGA alone. We believe such a product would be well received in the glaucoma market, especially for use in patients with higher IOPs that currently use two or more glaucoma drugs to lower IOP.

Our second product candidate is a combination of *trabodenoson* with a PGA, *latanoprost*, to create an FDC. While our FDC has not yet been formulated or administered to humans, we expect that *trabodenoson* will not adversely affect the safety profile of *latanoprost*, or any other

currently-approved PGA, because of its favorable safety and tolerability profile. We believe that *trabodenoson*'s mechanism for lowering IOP is likely to complement the mechanism of action of *latanoprost* and other PGAs, which work primarily on the secondary uveoscleral outflow, because *trabodenoson* is believed to act through the TM, the largest aqueous humor outflow path in the eye. In fact, our IOP-lowering studies in cynomolgus monkeys have shown that IOP-lowering is significantly better when the eye is treated with both *trabodenoson* and *latanoprost*, as compared to treatment with *latanoprost* alone. Moreover, *trabodenoson* appears to have a sufficiently long duration of action, which we believe may allow it to be effectively dosed QD in conjunction with *latanoprost* as an FDC. Assuming the *trabodenoson* safety profile remains favorable, a *trabodenoson-latanoprost* FDC therapy could present a much improved risk/benefit profile over other combinations of currently-approved PGAs and non-PGAs.

Trabodenoson for Optic Neuropathy

The neuroprotective potential of *trabodenoson* is supported by the basic biology of adenosine, which has shown that the stimulation of the A1 receptor can protect tissues of the central nervous system. While we have not yet conducted a formal program of studies to prove neuroprotection, we plan to study the potential of *trabodenoson* monotherapy and our FDC product candidate to slow the loss of vision significantly more than attributable to IOP lowering alone, either in glaucoma patients or in other rarer forms of optic nerve neuropathies.

Clinical Development Plan

Our planned Phase 3 program for *trabodenoson* as a monotherapy is expected to incorporate both the FDA-acceptable clinical endpoint of IOP, and to include studies with three months of treatment, both of which are well-known and accepted standards for pivotal trials for glaucoma. We are planning an End-of-Phase 2 meeting with the FDA in the first half of 2015 to discuss our Phase 3 program for *trabodenoson* monotherapy and to confirm the design and endpoints for the Phase 3 pivotal trials. *Timolol*, a non-PGA, will be used as the positive control in the Phase 3 pivotal trials due to its long history as a glaucoma therapy and the large amount of clinical data available on the drug, making it the comparator of choice in most recent Phase 3 trials in glaucoma. We plan to start our Phase 3 program for *trabodenoson* monotherapy in mid-2015, and we expect to report top-line data from the first pivotal trial in the program by late 2016 or early 2017, with the second pivotal trial being completed in 2017. After completion of the long-term monotherapy safety study, we plan to submit an NDA. We are planning to commence our Phase 3 program for the FDC of *trabodenoson* and *latanoprost* in 2017.

Our Strategy

Our goal is to become a leading biopharmaceutical company focused on the discovery, development and commercialization of novel therapies to treat glaucoma. The key elements of our strategy are as follows:

- Complete clinical development and seek marketing approval for our lead product candidate, *trabodenoson* monotherapy;
- Complete clinical development and seek marketing approval of an FDC product that includes both *trabodenoson* and *latanoprost*;
- Establish a specialty sales force to maximize the commercial potential of *trabodenoson* in the United States; and
- Evaluate the potential of *trabodenoson* to slow the loss of vision associated with glaucoma or for additional ophthalmic indications.

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 currently have no source of revenue and may never become profitable.
- We depend substantially on the success of our product candidates, particularly *trabodenoson* monotherapy and *trabodenoson* FDC, which are still in development. If we are unable to successfully commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.
- We will need to obtain additional financing to fund our operations and, if we are unable to obtain such financing, we may be unable to complete the development and commercialization of our primary product candidates.
- We have not obtained regulatory approval for any of our product candidates in the United States or in any other country, and we cannot guarantee that we will ever have marketable products.
- We have not yet successfully formulated, and may be unable to formulate or manufacture our fixed-dose combination product candidate in a way that is suitable for clinical or commercial use. Any such delay or failure could materially harm our commercial prospects, result in higher costs and deprive us of product candidate revenues.
- Our product candidates may have undesirable adverse effects, which may delay or prevent regulatory approval or, if approval is received, require our products to be taken off the market, require them to include safety warnings or otherwise limit their sales.
- If we are unable to effectively establish a direct sales force in the United States, our business may be harmed.
- We face competition from established branded and generic pharmaceutical companies and if our competitors are able to develop and market products that are preferred over our products, our commercial opportunity will be reduced or eliminated.
- The commercial success of our product candidates will depend on the degree of market acceptance among ophthalmologists and optometrists, patients, patient advocacy groups, third-party payors and the medical community.
- If we fail to obtain and sustain coverage and an adequate level of reimbursement for our product candidates by third-party payors, potential future sales would be materially adversely affected.
- We may not be able to protect our proprietary technology in the marketplace.
- We will need to significantly increase the size of our organization, and we may experience difficulties in managing growth.

Company and Other Information

We were incorporated under the laws of the State of Delaware on July 7, 1999. Our principal executive office is located at 131 Hartwell Avenue, Suite 105, Lexington, Massachusetts, and our telephone number is (781) 676-2100. Our website address is www.inotekpharma.com. We do not incorporate the information on or accessible through our website into this prospectus, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus. The reference to our website is an inactive textual reference only and is not a hyperlink.

All trademarks or trade names referred to in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and ™ symbols, but such references should not be construed as

any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies' trademarks and trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

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, and we may remain an emerging growth company for up to five years. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure and other requirements that are applicable to other public companies that are not emerging growth companies. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

The Offering

Common stock offered by us	shares
Common stock to be outstanding immediately after this offering	shares (shares if the underwriters exercise their option to purchase additional shares in full)
Underwriters' option to purchase additional shares	shares
Use of proceeds	We estimate that we will receive net proceeds from this offering of approximately $ million, or $ million, if the underwriters exercise their option to purchase additional shares in full, based upon an assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering to fund the continued development of our product candidates and for other general corporate purposes. See "Use of Proceeds."
Risk factors	You should carefully read "Risk Factors" in this prospectus for a discussion of factors that you should consider before deciding to invest in our common stock.
Proposed NASDAQ Global Market symbol	"ITEK"

The number of shares of our common stock to be outstanding after this offering is based on 34,590,552 shares of our common stock outstanding as of June 30, 2014, which assumes the conversion of all of our outstanding 25,097,103 shares of preferred stock, including all accrued and unpaid dividends thereon, into 30,450,953 shares of common stock, which will occur immediately prior to the closing of this offering, and excludes:

- 48,137 shares of common stock issuable upon the exercise of stock options at a weighted-average exercise price of $10.00 per share;
- 1,081,136 shares of common stock issuable upon the exercise of warrants outstanding, 852,230 of which have an exercise price of $0.01 per share and which are exercisable for preferred stock prior to the closing of this offering and will terminate upon the closing of this offering, and 228,906 of which have an exercise price of $1.529 per share, and which are exercisable for preferred stock prior to the closing of this offering and are exercisable for common stock upon the closing of this offering; and
- shares of common stock reserved for future issuance under our 2014 Stock Option and Incentive Plan, or the 2014 Plan.

Unless otherwise indicated, all information in this prospectus reflects or assumes the following:

- the filing and effectiveness of our amended and restated certificate of incorporation and the adoption of our amended and restated bylaws, which will occur immediately prior to the closing of this offering;
- the conversion of all of our outstanding 25,097,103 shares of preferred stock, including all accrued and unpaid dividends thereon, into 30,450,953 shares of common stock upon the closing of this offering;
- no issuance or exercise of stock options or warrants on or after June 30, 2014; and
- no exercise by the underwriters of their option to purchase up to an additional shares of common stock in this offering to cover overallotments, if any.

Summary Financial Data

The summary statements of operations data for the years ended December 31, 2012 and 2013 are derived from our audited financial statements included elsewhere in this prospectus. The summary statements of operations data for the six months ended June 30, 2013 and 2014, and the summary balance sheet data as of June 30, 2014, have been derived from our unaudited financial statements included elsewhere in this prospectus. Our unaudited financial statements have been prepared on a basis consistent with our audited financial statements included in this prospectus and, in the opinion of management, reflect all adjustments, consisting only of normal and recurring adjustments, necessary for a fair presentation of such financial data. You should read this summary financial data together with our audited financial statements and related notes included elsewhere in this prospectus and the information under the captions "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." Our historical results are not necessarily indicative of our future results, and our operating results for the six-month period ended June 30, 2014 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2014 or any other interim periods or any future year or period.

	Year Ended December 31,		Six Months Ended June 30,	
(in thousands, except share and per share data)	2012	2013	2013	2014
			(unaudited)	
Statements of Operations Data:				
Operating expenses:				
Research and development	$ (3,542)	$ (5,330)	$ (2,304)	$ (3,412)
General and administrative	(2,307)	(1,324)	(1,021)	(494)
Loss from operations	(5,849)	(6,654)	(3,325)	(3,906)
Other income	4	3	–	–
Interest expense	(213)	(884)	(388)	(491)
Change in fair value of warrant liabilities	–	(81)	–	(598)
Net loss	$ (6,058)	$ (7,616)	$ (3,713)	$ (4,995)
Net loss per common share—basic and diluted	$ (1.98)	$ (2.48)	$ (1.18)	$ (1.70)
Weighted-average common shares outstanding—basic and diluted	4,124,880	4,131,863	4,124,880	4,139,599
Pro forma net loss per common share—basic and diluted (unaudited)(1)		$ (0.35)		$ (0.21)
Pro forma weighted-average common shares outstanding—basic and diluted (unaudited)		29,413,014		33,796,398

(in thousands)	As of June 30, 2014 Actual (Unaudited)	Pro Forma(2) (Unaudited)	Pro Forma As Adjusted(3)(4) (Unaudited)
Balance Sheet Data:			
Cash and cash equivalents	$ 8,881	$ 8,881	
Total assets	8,923	8,923	
Notes payable—current portion	2,899	2,899	
Notes payable, net of current portion	4,012	4,012	
Warrant liabilities	2,486	—	
Total liabilities	11,576	9,090	
Series AA redeemable convertible preferred stock	42,715	—	
Accumulated deficit	(123,505)	(123,505)	
Total stockholders' deficit	(45,916)	(167)	

(1) See Note 2 to our consolidated financial statements included elsewhere in this prospectus for an explanation of the method used to calculate the historical and pro forma net loss per share, basic and diluted, and the number of shares used in the computation of the per share amounts.

(2) Pro forma column in the balance sheet data table above reflects (a) the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 30,450,953 shares of common stock immediately prior to the closing of this offering and (b) the filing and effectiveness of our amended and restated certificate of incorporation, which will occur immediately prior to the closing of this offering.

(3) Pro forma as adjusted column in the balance sheet data table above gives effect to (a) the pro forma adjustments set forth above and (b) the sale and issuance by us of shares of our common stock in this offering, based upon the assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

(4) A $1.00 increase (decrease) in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the amount of our cash and cash equivalents, total assets and total stockholders' equity by $, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. An increase (decrease) of one million shares offered by us would increase (decrease) the amount of our cash and cash equivalents, total assets and total stockholders' equity by $, assuming the assumed initial public offering price remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

RISK FACTORS

An investment in our common stock involves a high degree of risk. We operate in an industry that involves numerous risks and uncertainties. The risks and uncertainties described below may change over time and other risks and uncertainties, including those that we do not currently consider material, may impair our business. If any of the risks discussed below actually occur, our business, financial condition, operating results or cash flows could be materially adversely affected. This could cause the trading price of our common stock to decline, and you may lose all or part of your investment.

Risks Related to Our Financial Position and Need for Additional Capital

We currently have no source of revenue and may never become profitable.

We are a clinical-stage biopharmaceutical company with a limited operating history. Our ability to generate revenue and become profitable depends upon our ability to successfully complete the development of our product candidates for the treatment of glaucoma and obtain the necessary regulatory approvals for our product candidates. We have never been profitable, have no products approved for commercial sale and to date have not generated any revenue from product sales. Even if we receive regulatory approval for the sale of our product candidates, we do not know when such product candidates will generate revenue, if at all. Our ability to generate product revenue depends on a number of factors, including our ability to:

- successfully complete clinical development, and receive regulatory approval, for our product candidates, including *trabodenoson* monotherapy and *trabodenoson* with *latanoprost* as a fixed-dose combination, or FDC;
- set an acceptable price for our product candidates and obtain coverage and adequate reimbursement from third-party payors;
- establish sales, marketing and distribution systems for our product candidates;
- add operational, financial and management information systems and personnel, including personnel to support our clinical, manufacturing and planned future commercialization efforts;
- have commercial quantities of our product candidates manufactured at acceptable cost levels;
- successfully market and sell our product candidates in the United States and enter into partnerships or other arrangements to commercialize our product candidates outside the United States; and
- maintain, expand and protect our intellectual property portfolio.

In addition, because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses, or when, or if, we will be able to achieve or maintain profitability. In addition, our expenses could increase beyond expectations if we are required by the U.S. Food and Drug Administration, or FDA, and comparable non-U.S. regulatory authorities, or other regulatory authorities to perform studies or clinical trials in addition to those that we currently anticipate. Even if our product candidates are approved for commercial sale, we anticipate incurring significant costs associated with the commercial launch of these products.

Our ability to become and remain profitable depends on our ability to generate revenue. Even if we are able to generate revenues from the sale of our product candidates, we may not become profitable and may need to obtain additional funding to continue operations. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce our operations. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We have a history of net losses and anticipate that we will continue to incur net losses for the foreseeable future.

We have a history of losses and anticipate that we will continue to incur net losses for the foreseeable future. Our net losses were $6.1 million and $7.6 million for the years ended December 31, 2012 and 2013, respectively. Our net losses were $3.7 million and $5.0 million for the six months ended June 30, 2013 and 2014, respectively. As of June 30, 2014, we had an accumulated deficit of $123.5 million.

Investment in pharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that a product candidate will fail to gain regulatory approval or become commercially viable. We have devoted most of our financial resources to research and development, including our non-clinical development activities and clinical trials. We are not currently generating revenues, and we cannot estimate with precision the extent of our future losses. We do not currently have any products that are available for commercial sale and we may never generate revenue from selling products or achieve profitability. We expect to continue to incur substantial and increasing losses through the projected commercialization of our product candidates. None of our product candidates have been approved for marketing in the United States and may never receive such approval. As a result of these factors, we are uncertain when or if we will achieve profitability and, if so, whether we will be able to sustain it. Our ability to produce revenue and achieve profitability is dependent on our ability to complete the development of our product candidates, obtain necessary regulatory approvals, and have our products manufactured and successfully marketed. We cannot assure you that we will be profitable even if we successfully commercialize our products. Failure to become and remain profitable may adversely affect the market price of our common stock and our ability to raise capital and continue operations.

We have financed our operations with a combination of private and public grants and contracts and equity and preferred stock offerings. From 1997 to 2004, we have received non-dilutive funding totaling over $50 million through federal and private grants and contracts. Since 2004, we have raised additional equity capital with funding from biotechnology and pharmaceutical investors. In February 2004, we completed the sale of approximately $20 million of Series A preferred stock. In October 2005, we completed the sale of $35 million of Series B preferred stock. In October of 2007, we completed the sale of approximately $24 million of Series C preferred. In June 2011, we completed the sale of an aggregate of approximately $23.5 million of Series AA preferred stock in four separate closings during the preceding year. In February 2013, we completed the sale of approximately $3.5 million of convertible promissory notes in three separate closings during the preceding eight months. In July 2013, we completed the sale of an additional approximately $13.5 million of Series AA preferred stock, including the conversion of the convertible promissory notes, in two separate closings during the previous two months. Our product candidates will require the completion of regulatory review, significant marketing efforts and substantial investment before they can provide us with any revenue.

We expect our research and development expenses to continue to be significant in connection with our ongoing and planned Phase 2 clinical trials and our planned Phase 3 program. In addition, if we obtain regulatory approval for our product candidates, we expect to incur increased sales and marketing expenses. As a result, we expect to continue to incur significant and increasing operating losses and negative cash flows for the foreseeable future. These losses have had and will continue to have a material adverse effect on our stockholders' deficit, financial position, cash flows and working capital.

We will need to obtain additional financing to fund our operations and, if we are unable to obtain such financing, we may be unable to complete the development and commercialization of our primary product candidates.

Our operations have consumed substantial amounts of cash since inception. At June 30, 2014, our cash and cash equivalents were $8.9 million. We estimate that the net proceeds from this offering will be approximately $ million, based on the initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We believe that the net proceeds from this offering, together with existing cash and cash equivalents, will be sufficient to fund our projected operating requirements for at least the next 18 months. We expect that these funds will not be sufficient to enable us to complete all necessary development or commercially launch our current product candidates. We will need to obtain additional financing to conduct additional trials for the approval of our drug candidates if requested by regulatory bodies, and complete the development of any additional product candidates we might acquire. Moreover, our fixed expenses such as rent, interest expense and other contractual commitments are substantial and are expected to increase in the future.

Adequate additional funding may not be available to us on acceptable terms, or at all. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts. Our forecast of the period of time through which our financial resources will be adequate to support our operating requirements is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors, including the factors discussed elsewhere in this “Risk Factors” section. We have based this forecast on a number of assumptions that may prove to be wrong, and changing circumstances beyond our control may cause us to consume capital more rapidly than we currently anticipate.

Our future funding requirements will depend on many factors, including, but not limited to:

- the progress, timing, scope and costs of our clinical trials, including the ability to enroll patients in our planned and potential future clinical trials in a timely manner;
- the time and cost necessary to obtain regulatory approvals that may be required by regulatory authorities;
- our ability to successfully commercialize our product candidates;
- the amount of sales and other revenues from product candidates that we may commercialize, if any, including the selling prices for such product candidates and the availability of coverage and adequate reimbursement from third parties;
- selling and marketing costs associated with our product candidates, including the cost and timing of expanding our marketing and sales capabilities;
- the terms and timing of any potential future collaborations, licensing or other arrangements that we may establish;
- cash requirements of any future acquisitions and/or the development of other product candidates;
- the costs of operating as a public company;
- the time and cost necessary to respond to technological and market developments;
- the costs of maintaining and expanding our existing intellectual property rights; and
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

Until we can generate a sufficient amount of revenue, we may finance future cash needs through public or private equity offerings, license agreements, debt financings, collaborations, strategic

alliances, marketing or distribution arrangements or a combination thereof. Additional funds may not be available when we need them on terms that are acceptable to us, or at all. General market conditions or the market price of our common stock may not support capital raising transactions such as an additional public or private offering of our common stock or other securities. In addition, our ability to raise additional capital may be dependent upon our stock being quoted on the NASDAQ Global Market, or NASDAQ, or upon obtaining shareholder approval. There can be no assurance that we will be able to satisfy the criteria for continued listing on NASDAQ or that we will be able to obtain shareholder approval if it is necessary. If adequate funds are not available, we may be required to delay or reduce the scope of or eliminate one or more of our research or development programs or our commercialization efforts.

We may seek to access the public or private capital markets whenever conditions are favorable, even if we do not have an immediate need for additional capital at that time. In addition, if we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or to grant licenses on terms that may not be favorable to us. Our inability to obtain additional funding when we need it could seriously harm our business.

Additional capital that we may need to operate or expand our business may not be available. In addition, our agreements that govern our indebtedness contain covenants that restrict our ability to obtain additional capital and pursue business opportunities.

We may require additional capital to operate or expand our business. Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. For example, the agreements governing our indebtedness contain various restrictive covenants, including restrictions on our ability to dispose of assets, make acquisitions or investments, incur additional debt or liens, make distributions to our stockholders or enter into certain types of related party transactions, and any debt financing obtained by us in the future could involve further restrictive covenants, which may make it more difficult for us to obtain additional capital and pursue business opportunities. Moreover, our existing debt contains an optional prepayment penalty. If we raise additional funds through the issuance of equity or convertible securities, the percentage ownership of holders of our common stock could be significantly diluted and these newly issued securities may have rights, preferences or privileges senior to those of holders of our common stock. Furthermore, volatility in the credit or equity markets may have an adverse effect on our ability to obtain debt or equity financing or the cost of such financing. If we do not have funds available to enhance our solution, maintain the competitiveness of our technology and pursue business opportunities, this could have an adverse effect on our business, operating results and financial condition.

Risks Related to Development, Regulatory Approval and Commercialization

We depend substantially on the success of our product candidates, particularly trabodenoson monotherapy and trabodenoson FDC, which are still in development. If we are unable to successfully commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

Our business and the ability to generate revenue related to product sales, if ever, will depend on the successful development, regulatory approval and commercialization of our product candidates *trabodenoson* monotherapy and *trabodenoson* FDC, which are still in development, and other potential products we may develop or license. We have invested a significant portion of our efforts and financial resources in the development of our existing product candidates. The success of our product candidates will depend on several factors, including:

- successful completion of clinical trials, and the supporting non-clinical toxicology, formulation development, and manufacturing of supplies for the clinical program in accordance with current Good Manufacturing Practices, or cGMP;

- receipt of regulatory approvals from the FDA and other applicable regulatory authorities outside the United States;
- establishment of arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity;
- protecting our rights in our intellectual property;
- launching commercial sales of our product candidates, if and when approved;
- acceptance of any approved product by the medical community and patients;
- obtaining coverage and adequate reimbursement from third-party payors for product candidates, if and when approved;
- effectively competing with other products; and
- achieving a continued acceptable safety profile for our product candidates following regulatory approval, if and when received.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business and we may not be able to earn sufficient revenues and cash flows to continue our operations.

Our product candidates are *trabodenoson* as a monotherapy and as an FDC consisting of *trabodenoson* with a prostaglandin analog, or PGA. We have no other product candidates in our near term product pipeline. As a result, we are substantially dependent on the successful development and commercialization of *trabodenoson*. If the results of our chronic toxicology program were to identify a safety problem, or if our Phase 2 clinical trial or our upcoming pivotal trials of *trabodenoson* monotherapy were to demonstrate lack of efficacy in lowering intraocular pressure, or IOP, or any safety issues related to *trabodenoson*, our development strategy would be materially and adversely affected.

We have not obtained regulatory approval for any of our product candidates in the United States or in any other country.

We currently do not have any product candidates that have gained regulatory approval for sale in the United States or in any other country, and we cannot guarantee that we will ever have marketable products. Our business is substantially dependent on our ability to complete the development of, obtain regulatory approval for and successfully commercialize product candidates in a timely manner. We cannot commercialize product candidates in the United States without first obtaining regulatory approval to market each product from the FDA; similarly, we cannot commercialize product candidates outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. *Trabodenoson* is currently undergoing a Phase 2 trial in which we are testing *trabodenoson* co-administered with *latanoprost*. We are planning an End-of-Phase 2 meeting with the FDA for *trabodenoson* monotherapy in the first half of 2015 and expect to initiate a pivotal Phase 3 program in mid-2015, which will consist of two Phase 3 pivotal trials and a long-term safety study. We cannot predict whether our current Phase 2 trial or any future trials, including our planned long-term safety trial of *trabodenoson*, will be successful or whether regulators will agree with our conclusions regarding the preclinical studies and clinical trials we have conducted to date.

Before obtaining regulatory approvals for the commercial sale of any product candidate for a target indication, we must demonstrate in preclinical studies and well-controlled clinical trials, and, with respect to approval in the United States, to the satisfaction of the FDA, that the product candidate is safe and effective for use for that target indication and that the manufacturing facilities, processes and controls are adequate. In the United States, we have not submitted a New Drug Application, or NDA, for any of our product candidates. An NDA must include extensive preclinical and clinical data and supporting information to establish the product candidate's safety and effectiveness for each desired

indication. The NDA must also include significant information regarding the chemistry, manufacturing and controls for the product. Obtaining approval of an NDA is a lengthy, expensive and uncertain process, and approval may not be obtained. If we submit an NDA to the FDA, the FDA must decide whether to accept or reject the submission for filing. We cannot be certain that any submissions will be accepted for filing and review by the FDA.

Regulatory authorities outside of the United States, such as in Europe and Japan and in emerging markets, also have requirements for approval of drugs for commercial sale with which we must comply prior to marketing in those areas. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our product candidates. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and obtaining regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking non-U.S. regulatory approval could require additional non-clinical studies or clinical trials, which could be costly and time consuming. The non-U.S. regulatory approval process may include all of the risks associated with obtaining FDA approval. For all of these reasons, we may not obtain non-U.S. regulatory approvals on a timely basis, if at all.

The process to develop, obtain regulatory approval for and commercialize product candidates is long, complex and costly both inside and outside of the United States, and approval is never guaranteed. Even if our product candidates were to successfully obtain approval from the regulatory authorities, any approval might significantly limit the approved indications for use, or require that precautions, contraindications, or warnings be included on the product labeling, or require expensive and time-consuming post-approval clinical trials or surveillance as conditions of approval. Following any approval for commercial sale of our product candidates, certain changes to the product, such as changes in manufacturing processes and additional labeling claims, will be subject to additional FDA review and approval. Also, regulatory approval for any of our product candidates may be withdrawn. If we are unable to obtain regulatory approval for our product candidates in one or more jurisdictions, or any approval contains significant limitations, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed. Furthermore, we may not be able to obtain sufficient funding or generate sufficient revenue and cash flows to continue the development of any other product candidate in the future.

Regulatory approval may be substantially delayed or may not be obtained for one or all of our product candidates if regulatory authorities require additional time or studies to assess the safety and efficacy of our product candidates.

We may be unable to initiate or complete development of our product candidates on schedule, if at all. The timing for the completion of the studies for our product candidates will require funding beyond the proceeds of this offering. In addition, if regulatory authorities require additional time or studies to assess the safety or efficacy of our product candidates, we may not have or be able to obtain adequate funding to complete the necessary steps for approval for any or all of our product candidates. Preclinical studies and clinical trials required to demonstrate the safety and efficacy of our product candidates are time consuming and expensive and together take several years or more to complete. Delays in regulatory approvals or rejections of applications for regulatory approval in the United States, Europe, Japan or other markets may result from many factors, including:

- our inability to obtain sufficient funds required for a clinical trial;
- requests from regulatory authorities for additional analyses, reports, data, non-clinical and preclinical studies and clinical trials;
- questions from regulatory authorities regarding interpretations of data and results and the emergence of new information regarding our product candidates or other products;

- clinical holds, other regulatory objections to commencing or continuing a clinical trial or the inability to obtain regulatory approval to commence a clinical trial in countries that require such approvals;
- failure to reach agreement with the FDA or comparable non-US regulatory authorities regarding the scope or design of our clinical trials;
- our inability to enroll a sufficient number of patients who meet the inclusion and exclusion criteria in our clinical trials. For example, we are seeking patients with elevated levels of IOP for our clinical trials, which are more difficult to find;
- our inability to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- our inability to reach agreements on acceptable terms with prospective contract research organizations, or CROs, and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- our inability to identify and maintain a sufficient number of sites, many of which may already be engaged in other clinical trial programs, including some that may be for the same indications targeted by our product candidates;
- any determination that a clinical trial presents unacceptable health risks;
- lack of adequate funding to continue the clinical trial due to unforeseen costs or other business decisions;
- our inability to obtain approval from Institutional Review Boards, or IRBs, to conduct clinical trials at their respective sites;
- our inability to manufacture in a timely manner or obtain from third parties sufficient quantities or quality of the product candidates or other materials required for a clinical trial;
- difficulty in maintaining contact with patients after treatment, resulting in incomplete data; and
- unfavorable or inconclusive results of clinical trials and supportive non-clinical studies, including unfavorable results regarding the effectiveness of product candidates during clinical trials.

Changes in regulatory requirements and guidance may also occur and we may need to amend clinical trial protocols submitted to applicable regulatory authorities to reflect these changes. Amendments may require us to resubmit clinical trial protocols to IRBs for re-examination, which may impact the costs, timing or successful completion of a clinical trial.

As a result of our planned End-of-Phase 2 meeting with the FDA for *trabodenoson* in the first half of 2015, the FDA may require us to conduct additional clinical trials before we commence our Phase 3 pivotal trials and long-term safety study or they may require us to increase the size of or change the design of our planned pivotal trials. In addition, if the FDA requires us to change the design of our planned pivotal trials, the actual costs of these trials may be greater than what we estimated based on our current expectations regarding the design of these trials. If we are required to conduct additional clinical trials or other studies with respect to any of our product candidates beyond those that we initially contemplated, if we are unable to successfully complete our clinical trials or other studies or if the results of these studies are not positive or are only modestly positive, we may be delayed in obtaining regulatory approval for that product candidate, we may not be able to obtain regulatory approval at all or we may obtain approval for indications that are not as broad as intended. Our product development costs will also increase if we experience delays in testing or approvals and we may not have sufficient funding to complete the testing and approval process. Significant clinical trial delays could allow our competitors to bring products to market before we do and impair our ability to commercialize our products if and when approved. If any of this occurs, our business will be materially harmed.

We have not yet successfully formulated, and may be unable to formulate or manufacture our fixed-dose combination product candidate in a way that is suitable for clinical or commercial use. Any such delay or failure could materially harm our commercial prospects, result in higher costs and deprive us of product candidate revenues.

We are currently conducting a Phase 2 trial to evaluate the efficacy, tolerability and safety of *trabodenoson* when co-administered with commercially-available *latanoprost* eye drops. However, we have not yet formulated our FDC product candidate to include these two drugs in a single combination dose, and we may never be able to formulate or manufacture our FDC product candidate in a way that is suitable for clinical or commercial use. Any delay or failure to develop a suitable product formulation or manufacturing process for our FDC product candidate could materially harm our commercial prospects, result in higher costs or deprive us of potential product revenues.

Failure can occur at any stage of clinical development. If the clinical trials for our product candidates are unsuccessful, we could be required to abandon development.

A failure of one or more clinical trials can occur at any stage of testing for a variety of reasons. The outcome of preclinical testing and early clinical trials may not be predictive of the outcome of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. In addition, adverse events may occur or other risks may be discovered in Phase 2 or Phase 3 clinical trials that will cause us to suspend or terminate our clinical trials. In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes in or adherence to trial protocols, differences in size and type of the patient populations and the rates of dropout among clinical trial participants. To date, we have only exposed 183 clinical trial subjects to *trabodenoson*. The FDA expects that a total of at least 1,500 patients are exposed to at least a single dose of *trabodenoson* before submission of an NDA, and the complete NDA submission package must also contain safety data from at least 300 patients treated with *trabodenoson* for at least six months, and at least 100 patients treated for at least a year. Our future clinical trial results therefore may not demonstrate safety and efficacy sufficient to obtain regulatory approval for our product candidates. Moreover, we still need to evaluate the long-term safety effects of our product candidates, the results of which could adversely affect our clinical development program.

Flaws in the design of a clinical trial may not become apparent until the clinical trial is well-advanced. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support regulatory approval. In addition, clinical trials often reveal that it is not practical or feasible to continue development efforts. Further, we have never submitted an NDA for any product candidates.

We may voluntarily suspend or terminate our clinical trials if at any time we believe that they present an unacceptable risk to participants. Further, regulatory agencies, IRBs or data safety monitoring boards may at any time order the temporary or permanent discontinuation of our clinical trials or request that we cease using investigators in the clinical trials if they believe that the clinical trials are not being conducted in accordance with applicable regulatory requirements, or that they present an unacceptable safety risk to participants.

If the results of our clinical trials for our current product candidates or clinical trials for any future product candidates do not achieve the primary efficacy endpoints or demonstrate unexpected safety issues, the prospects for approval of our product candidates will be materially adversely affected. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have failed to achieve similar results in later clinical trials, including longer term trials, or have failed to obtain regulatory approval of their product candidates. Many compounds that initially showed promise in clinical trials or earlier stage testing have later been found to cause

undesirable or unexpected adverse effects that have prevented further development of the compound. In addition, we have typically only tested our product candidates in a single eye, which may not accurately predict the efficacy or safety of our product candidates when dosed in both eyes. Our current Phase 2 trial and our planned Phase 3 pivotal trials of *trabodenoson* monotherapy may not produce the results that we expect. Our clinical trials are also designed to test the use of *trabodenoson* in combination with *latanoprost* as an add-on therapy. Accordingly, the efficacy of our primary product candidates may not be similar or correspond directly to their efficacy when used as a monotherapy. Our current product candidates remain subject to the risks associated with clinical drug development as indicated above.

In addition to the circumstances noted above, we may experience numerous unforeseen events that could cause our clinical trials to be delayed, suspended or terminated, or which could delay or prevent our ability to receive regulatory approval or commercialize our product candidates, including:

- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or implement a clinical hold;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators or IRBs may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- we may elect or be required to suspend or terminate clinical trials of our product candidates based on a finding that the participants are being exposed to health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and
- our product candidates may have undesirable adverse effects or other unexpected characteristics.

If we elect or are required to suspend or terminate a clinical trial of any of our product candidates, our commercial prospects will be adversely impacted and our ability to generate product revenues may be delayed or eliminated.

Our product candidates may have undesirable adverse effects, which may delay or prevent regulatory approval or, if approval is received, require our products to be taken off the market, require them to include safety warnings or otherwise limit their sales.

Unforeseen adverse effects from any of our product candidates could arise either during clinical development or, if approved, after the approved product has been marketed. In particular, we are aware of the known potential of adenosine and adenosine-like drugs to affect the heart if present in the systematic circulation at high enough levels.

Any undesirable adverse effects that may be caused by our product candidates could interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA and comparable non-U.S. regulatory authorities for any or all targeted indications, and in turn prevent us from commercializing our product candidates and generating revenues from their sale. In addition, if

any of our product candidates receives regulatory approval and we or others later identify undesirable adverse effects caused by the product, we could face one or more of the following consequences:

- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication, or other labeling changes;
- regulatory authorities may withdraw their approval of the product;
- regulatory authorities may seize the product;
- we may be required to change the way that the product is administered, conduct additional clinical trials or recall the product;
- we may be subject to litigation or product liability claims, fines, injunctions, or criminal penalties; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product or could substantially increase the costs and expenses of commercializing such product, which in turn could delay or prevent us from generating significant revenues from its sale.

Trabodenoson is an adenosine mimetic. Adenosine is used therapeutically to manage cardiovascular arrhythmias, such as paroxysmal supraventricular tachycardia, a type of accelerated heart rate. All of our data to date reflects that *trabodenoson* does not have systemic effects, including no impact on the cardiovascular system when dosed in the eye. However, we are still conducting additional trials for *trabodenoson* and systemic effects may arise in future trials. Furthermore, if *trabodenoson* has the perception of having potential adverse effects because it is an adenosine mimetic, it may be negatively viewed by ophthalmologists and optometrists, patients, patient advocacy groups, third-party payors and the medical community which would adversely affect the market acceptance of our product candidates. In addition, the use of our product candidates outside the indications cleared for use, or off-label use, or the use of our product candidate in an inappropriate manner, may increase the risk of injury to patients. Clinicians may use our products for off-label uses, as the FDA does not restrict or regulate a clinician’s choice of treatment within the practice of medicine. Off-label use of our products may increase the risk of product liability claims against us. Product liability claims are expensive to defend and could divert our management’s attention and result in substantial damage awards against us.

If our product candidates receive regulatory approval, we will be subject to ongoing regulatory requirements and we may face future development, manufacturing and regulatory difficulties.

Our product candidates, if approved, will also be subject to ongoing regulatory requirements for labeling, packaging, storage, advertising, promotion, sampling, record-keeping, submission of safety and other post-market approval information, importation and exportation. In addition, approved products, manufacturers and manufacturers’ facilities are required to comply with extensive FDA and European Medicines Agency, or EMA, requirements and the requirements of other similar agencies, including ensuring that quality control and manufacturing procedures conform to cGMP requirements. As such, we and our potential future contract manufacturers will be subject to continual review and periodic inspections to assess compliance with cGMPs. Accordingly, we and others with whom we work will be required to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. We will also be required to report certain adverse reactions and production problems, if any, to the FDA, EMA and other similar foreign agencies and to comply with certain requirements concerning advertising and promotion for our product candidates. Promotional communications with respect to prescription drugs also are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product’s approved labeling. Accordingly, once approved, we may not promote our products, if any, for indications or uses for which they are not approved.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, it may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If our product candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- require product recalls;
- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners;
- require us or our potential future collaborators to enter into a consent decree or permanent injunction, which can include shutdown of manufacturing facilities, imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- impose other administrative or judicial civil or criminal penalties or pursue criminal prosecution;
- withdraw regulatory approval;
- refuse to approve pending applications or supplements to approved applications filed by us or by our potential future collaborators;
- impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products.

If we are unable to effectively establish a direct sales force in the United States, our business may be harmed.

We currently do not have an established sales organization and do not have a marketing or distribution infrastructure. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. If *trabodenoson* receives marketing approval in the United States, we plan to commercialize it by establishing a glaucoma-focused specialty sales force of approximately 150 people targeting high-prescribing ophthalmologists and optometrists throughout the United States. We will need to incur significant additional expenses and commit significant additional time and management resources to establish and train a sales force to market and sell our products. We may not be able to successfully establish these capabilities despite these additional expenditures.

Factors that may inhibit our efforts to successfully establish a sales force include:

- our inability to compete with other pharmaceutical companies to recruit, hire, train and retain adequate numbers of effective sales and marketing personnel with requisite knowledge of our target market;
- the inability of sales personnel to obtain access to adequate numbers of ophthalmologists and optometrists to prescribe any future approved products;
- unforeseen costs and expenses associated with creating an independent sales and marketing organization; and
- a delay in bringing products to market after efforts to hire and train our sales force have already commenced.

In the event we are unable to successfully market and promote our products, our business may be harmed.

We currently intend to explore the licensing of commercialization rights or other forms of collaboration outside of the United States, which will expose us to additional risks of conducting business in international markets.

The non-U.S. markets are an important component of our growth strategy. If we fail to obtain licenses or enter into collaboration arrangements with selling parties, or if these parties are not successful, our revenue-generating growth potential will be adversely affected. Moreover, international business relationships subject us to additional risks that may materially adversely affect our ability to attain or sustain profitable operations, including:

- efforts to enter into collaboration or licensing arrangements with third parties in connection with our international sales, marketing and distribution efforts may increase our expenses or divert our management's attention from the acquisition or development of product candidates;
- changes in a specific country's or region's political and cultural climate or economic condition;
- differing regulatory requirements for drug approvals and marketing internationally, which could result in our being required to conduct additional clinical trials or other studies before being able to successfully commercialize our product candidates in any jurisdiction outside the United States;
- difficulty of effective enforcement of contractual provisions in local jurisdictions;
- potentially reduced protection for intellectual property rights;
- potential third-party patent rights in countries outside of the United States;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability, particularly in non-U.S. economies and markets, including several countries in Europe;
- compliance with tax, employment, immigration and labor laws for employees traveling abroad;
- the effects of applicable foreign tax structures and potentially adverse tax consequences;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incidental to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market (with low or lower prices) rather than buying them locally;
- failure of our employees and contracted third parties to comply with Office of Foreign Asset Control rules and regulations and the Foreign Corrupt Practices Act;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters, including earthquakes, volcanoes, typhoons, floods, hurricanes and fires.

These and other risks may materially adversely affect our ability to attain or sustain revenue from international markets.

We face competition from established branded and generic pharmaceutical companies and if our competitors are able to develop and market products that are preferred over our products, our commercial opportunity will be reduced or eliminated.

The development and commercialization of new drug products is highly competitive. We face competition from established branded and generic pharmaceutical companies, smaller biotechnology and pharmaceutical companies, as well as from academic institutions, government agencies and private and public research institutions, which may in the future develop products to treat glaucoma. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. Many of our competitors have

significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Glaukos Corporation recently commercialized a trabecular micro-bypass stent that is implanted in the eye during cataract surgery and allows fluid to flow from the anterior of the eye into the collecting channels, bypassing the TM. In addition, early-stage companies that are also developing glaucoma treatments may prove to be significant competitors, such as Aerie Pharmaceuticals, Inc., which is developing a Rho kinase/norepinephrine transport inhibitor. We expect that our competitors will continue to develop new glaucoma treatments, which may include eye drops, oral treatments, surgical procedures, implantable devices or laser treatments. Other early-stage companies may also compete through collaborative arrangements with large and established companies. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Our commercial opportunity will be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer adverse effects, are more convenient or are less expensive than our product candidates. The market for glaucoma prescriptions is highly competitive and is currently dominated by generic drugs, such as *latanoprost* and *timolol*, and additional products are expected to become available on a generic basis over the coming years. If any of our product candidates are approved, we expect that they will be priced at a premium over competitive generic products and consistent with other branded glaucoma drugs.

If our competitors market products that are more effective, safer, have fewer side effects or are less expensive than our product candidates or that reach the market sooner than our potential future products, if any, we may not achieve commercial success.

The commercial success of our product candidates will depend on the degree of market acceptance among ophthalmologists and optometrists, patients, patient advocacy groups, third-party payors and the medical community.

Our product candidates may not gain market acceptance among ophthalmologists and optometrists, patients, patient advocacy groups, third-party payors and the medical community. There are a number of available therapies marketed for the treatment of glaucoma. Some of these drugs are branded and subject to patent protection, but most others, including *latanoprost* and many beta blockers, are available on a generic basis. Many of these approved drugs are well established therapies and are widely accepted by ophthalmologists and optometrists, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products. Additionally, in patients with normal tension glaucoma whose IOP falls into the normal range, IOP is generally much more difficult to reduce. In these patients, *trabodenoson* may offer little or no clinical benefit, which may ultimately limit its utility in this subpopulation of glaucoma patients. The degree of market acceptance of our product candidates will depend on a number of factors, including:

- the market price, affordability and patient out-of-pocket costs of our product candidates relative to other available products, which are predominantly generics;
- the effectiveness of our product candidates as compared with currently available products and any products that may be approved in the future;
- patient willingness to adopt our product candidates in place of current therapies;
- varying patient characteristics including demographic factors such as age, health, race and economic status;
- changes in the standard of care for the targeted indications for any of our product candidates;
- the prevalence and severity of any adverse effects or perception of any potential side effects;
- limitations or warnings contained in a product candidate's FDA-approved labeling;
- limitations in the approved clinical indications for our product candidates;
- relative convenience and ease of administration;
- the strength of our selling, marketing and distribution capabilities;

- the quality of our relationship with patient advocacy groups;
- sufficient third-party coverage and reimbursement; and
- product liability claims.

In addition, the potential market opportunity for our product candidates is difficult to precisely estimate. Our estimates of the potential market opportunity for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research reports and other surveys. If any of these assumptions proves to be inaccurate, then the actual market for our product candidates could be smaller than our estimates of our potential market opportunity. If the actual market for our product candidates is smaller than we expect, our product revenue may be limited, and it may be more difficult for us to achieve or maintain profitability. If we fail to achieve market acceptance of our product candidates in the United States and abroad, our revenue will be more limited and it will be more difficult to achieve profitability.

If we fail to obtain and sustain coverage and an adequate level of reimbursement for our product candidates by third-party payors, potential future sales would be materially adversely affected.

The course of treatment for glaucoma patients includes primarily older drugs, and the leading products for the treatment of glaucoma currently in the market, including *latanoprost* and *timolol*, are available as generic brands. There will be no commercially viable market for our product candidates without coverage and adequate reimbursement from third-party payors, and any coverage and reimbursement policy may be affected by future healthcare reform measures. We cannot be certain that coverage and adequate reimbursement will be available for our product candidates or any other future product candidates we develop. Additionally, even if there is a commercially viable market, if the level of reimbursement is below our expectations, our anticipated revenue and gross margins will be adversely affected.

Third-party payors, such as government or private healthcare insurers, carefully review and increasingly question and challenge the coverage of and the prices charged for drugs. Reimbursement rates from private health insurance companies vary depending on the company, the insurance plan and other factors. Reimbursement rates may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. A current trend in the U.S. healthcare industry is toward cost containment. Large public and private payors, managed care organizations, group purchasing organizations and other similar organizations are exerting increasing influence on decisions regarding the use of, and reimbursement levels for, particular treatments. Such third-party payors, including Medicare, may question the coverage of, and challenge the prices charged for, medical products and services, and many third-party payors limit coverage of or reimbursement for newly approved healthcare products. In particular, third-party payors may limit the covered indications. Cost-control initiatives could decrease the price we might establish for our product candidates, which could result in product revenues being lower than anticipated. We believe our drugs will be priced significantly higher than existing generic drugs and consistently with current branded drugs. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. If we are unable to show a significant benefit relative to existing generic drugs, Medicare, Medicaid and private payors may not be willing to cover or provide adequate reimbursement for our drugs, which would significantly reduce the likelihood of them gaining market acceptance. In the United States, no uniform policy requirement for coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor.

We expect that private insurers will consider the efficacy, cost effectiveness, safety and tolerability of our product candidates in determining whether to approve coverage and set reimbursement levels for such products. Obtaining these approvals can be a time consuming and expensive process. Our business and prospects would be materially adversely affected if we do not receive approval for coverage and reimbursement of our product candidates from private insurers on a timely or satisfactory basis. Limitations on coverage and reimbursement could also be imposed by government payors, such as the local Medicare carriers, fiscal intermediaries, or Medicare Administrative Contractors. Further, Medicare Part D, which provides a pharmacy benefit to certain Medicare patients, does not require participating prescription drug plans to cover all drugs within a class of products. Our business could be materially adversely affected if private or governmental payors, including Medicare Part D prescription drug plans were to limit access to, or deny or limit reimbursement of, our product candidates or other potential products.

Reimbursement systems in international markets vary significantly by country and by region, and reimbursement approvals must be obtained on a country-by-country basis. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. For example, reimbursement in the European Union must be negotiated on a country-by-country basis and in many countries the product cannot be commercially launched until reimbursement is approved. The negotiation process in some countries can exceed 12 months. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our products to other available therapies.

If the prices for our product candidates decrease or if governmental and other third-party payors do not provide coverage and adequate reimbursement levels, our revenue, potential for future cash flows and prospects for profitability will suffer.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

The pricing of prescription pharmaceuticals is also subject to governmental control outside of the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

If we are found in violation of federal or state "fraud and abuse" laws or other healthcare laws, we may face penalties, which may adversely affect our business, financial condition and results of operation.

In the United States, we are subject to various federal and state healthcare "fraud and abuse" laws, including anti-kickback laws, false claims laws and other laws intended, among other things, to reduce fraud and abuse in federal and state healthcare programs. The Federal Anti-Kickback Statute makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration that is intended to induce the referral of business, including the purchase, lease, order or arranging for or recommending the purchase, lease or order of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as Medicare or Medicaid. Although we seek to structure our business arrangements in compliance with all applicable requirements, these laws are broadly written, and it is often difficult to determine precisely how the law will be applied in specific circumstances. Accordingly, it is possible that our practices may be challenged under the Federal Anti-Kickback Statute. The Federal False Claims Act prohibits anyone from, among other things, knowingly presenting or causing to be presented for payment to the government, including the federal healthcare

programs, claims for reimbursed drugs or services that are false or fraudulent. This statute has been interpreted to prohibit presenting claims for items or services that were not provided as claimed, or claims for medically unnecessary items or services. Many states have similar false claims laws. Cases have been brought under false claims laws alleging that off-label promotion of pharmaceutical products or the provision of kickbacks have resulted in the submission of false claims to governmental healthcare programs. In addition, private individuals have the ability to bring actions on behalf of the government under the Federal False Claims Act as well as under the false claims laws of several states. Under the Health Insurance Portability and Accountability Act of 1996, or HIPAA, we are prohibited from, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private payors, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services to obtain money or property of any healthcare benefit program.

Similarly, the civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

Additionally, the federal Physician Payments Sunshine Act within the Patient Protection and Affordable Care Act, as amended by the Health Care Education and Reconciliation Act, or collectively the ACA, and its implementing regulations, require that certain manufacturers of drugs, devices, biologics and medical supplies to report annually information related to certain payments or other transfers of value provided to physicians and teaching hospitals, and certain ownership and investment interests held by physicians and their immediate family members.

Many states have adopted laws similar to the aforementioned laws, some of which apply to the referral of patients for healthcare services reimbursed by any source, not just governmental payors. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 U.S. Department of Health and Human Services Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America's Code on Interactions with Healthcare Professionals. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state. There are ambiguities as to what is required to comply with these state requirements and if we fail to comply with an applicable state law requirement we could be subject to penalties.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, including the final omnibus rule published on January 25, 2013, imposes specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to business associates, defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Law enforcement authorities are increasingly focused on enforcing these laws, and it is possible that some of our practices may be challenged under these laws. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that the government could allege violations of, or convict us of violating, these laws. If we are found in violation of one of these laws, we could be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from governmental funded federal or state healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations. Were this to occur, our business, financial condition and results of operations and cash flows may be materially adversely affected.

Recently enacted and future legislation may increase the difficulty and cost of commercializing our product candidates and may affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay regulatory approval of our product candidates, restrict or regulate post-marketing activities and affect our ability to profitably sell our product candidates for which we obtain regulatory approval.

In March 2010, President Obama signed into law the ACA, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The ACA increased manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate amount for both branded and generic drugs and revised the definition of average manufacturer price, or AMP, which may also increase the amount of Medicaid drug rebates manufacturers are required to pay to states. The legislation also expanded Medicaid drug rebates, which previously had been payable only on fee-for-service utilization, to Medicaid managed care utilization, and created an alternative rebate formula for certain new formulations of certain existing products that is intended to increase the rebates due on those drugs. Further, the ACA imposed a significant annual fee on companies that manufacture or import branded prescription drug products and requires manufacturers to provide a 50% discount off the negotiated price of branded drugs dispensed to beneficiaries in the Medicare Part D coverage gap, referred to as the "donut hole." Substantial new provisions affecting compliance have also been enacted, including the Physician Payments Sunshine Act, as described above. Although it is too early to determine the full effect of the ACA, the new law appears likely to continue the downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach the required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2024 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability.

Legislative and regulatory proposals have been introduced at both the state and federal level to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We are not sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing approval testing and other requirements.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict whether future healthcare initiatives will be implemented at the federal or state level or in countries outside of the United States in which we may do business in the future, or the effect any future legislation or regulation will have on us.

If we face allegations of noncompliance with the law and encounter sanctions, our reputation, revenues and liquidity may suffer, and our products could be subject to restrictions or withdrawal from the market.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenues from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected. Additionally, if we are unable to generate revenues from our product sales, our potential for achieving profitability will be diminished and the capital necessary to fund our operations will be increased.

We may not be able to identify additional therapeutic opportunities for our product candidates or to expand our portfolio of products.

We may explore other therapeutic opportunities with *trabodenoson* and seek to commercialize a portfolio of new ophthalmic drugs in addition to our product candidates that we are currently developing. We have no potential products in our research and development pipeline other than those potential products that are formulations of *trabodenoson* or that apply *trabodenoson* for the treatment of other indications beyond glaucoma and other neuropathies.

Research programs to pursue the development of our product candidates for additional indications and to identify new potential products and disease targets require substantial technical, financial and human resources whether or not we ultimately are successful. Our research programs may initially show promise in identifying potential indications and/or potential products, yet fail to yield results for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential indications and/or potential products;
- product candidates may, after further study, be shown to have harmful adverse effects or other characteristics that indicate they are unlikely to be effective drugs; or
- it may take greater human and financial resources to identify additional therapeutic opportunities for our product candidates or to develop suitable potential products through internal research programs and clinical trials than we will possess, thereby limiting our ability to diversify and expand our product portfolio.

Because we have limited financial and managerial resources, we focus on research programs and product candidates for specific indications. As a result, we may forego or delay pursuit of opportunities with other potential products or for other indications that later prove to have greater commercial potential or a greater likelihood of success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities.

Accordingly, there can be no assurance that we will ever be able to identify additional therapeutic opportunities for our product candidates or to develop suitable potential products through internal research programs, which could materially adversely affect our future growth and prospects.

Risks Related to Our Reliance on Third Parties

We currently depend on third parties to conduct some of the operations of our clinical trials and other portions of our operations, and we may not be able to control their work as effectively as if we performed these functions ourselves.

We rely on third parties, such as contract research organizations, or CROs, clinical data management organizations, medical institutions and clinical investigators, to oversee and conduct our clinical trials, and to perform data collection and analysis of our product candidates. We expect to rely on these third parties to conduct clinical trials of any other potential products that we develop. These parties are not our employees and we cannot control the amount or timing of resources that they devote to our program. In addition, any CRO that we retain will be subject to the FDA's regulatory requirements or similar foreign standards and we do not have control over compliance with these regulations by these providers. Our agreements with third-party service providers are on trial-by-trial and project-by-project bases. Typically, we may terminate the agreements with notice and occasionally the third party service provider may terminate the agreement without notice. Typically, we are responsible for the third party's incurred costs and occasionally we have to pay cancellation fees. If any of our relationships with our third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. We also rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or regulatory approval of our product candidates or commercialization of our product candidates, producing additional losses and depriving us of potential product revenue.

Our reliance on these third parties for clinical development activities reduces our control over these activities but does not relieve us of our responsibilities, and we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan, the protocols for the trial and the FDA's regulations and international standards, referred to as Good Clinical Practice, or GCP, requirements, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Preclinical studies must also be conducted in compliance with other requirements, such as Good Laboratory Practice, or GLP, and the Animal Welfare Act. Managing performance of third-party service providers can be difficult, time consuming and cause delays in our development programs. We currently have a small number of employees, which limits the internal resources we have available to identify and monitor our third-party providers.

Furthermore, these third parties may conduct clinical trials for competing drugs or may have relationships with other entities, some of which may be our competitors. As such, the ability of these third parties to provide services to us may be limited by their work with these other entities. The use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated.

If these third parties do not successfully carry out their contractual duties or obligations and meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols according to regulatory requirements or for other reasons, our financial results and the commercial prospects for our current product candidates or our other potential products could be harmed, our costs could increase and our ability to obtain regulatory approval and commence product sales could be delayed.

We have no manufacturing capacity or experience and anticipate continued reliance on third-party manufacturers for the development and commercialization of our product candidates in accordance with manufacturing regulations.

We do not currently, nor currently intend to, operate manufacturing facilities for clinical or commercial production of our product candidates. We have no experience in drug formulation, and we lack the resources and the capabilities to manufacture our product candidates and potential products on a clinical or commercial scale. We do not intend to develop facilities for the manufacture of product candidates for clinical trials or commercial purposes in the foreseeable future. We currently rely on third-party manufacturers to produce the active pharmaceutical ingredient and final drug product for our clinical trials. We manage such production with all our vendors on a purchase order basis in accordance with applicable master service and supply agreements. We do not have long-term agreements with any of these or any other third-party suppliers. To the extent we terminate our existing supplier arrangements in the future and seek to enter into arrangements with alternative suppliers, we might experience a delay in our ability to obtain adequate supply for our clinical trials and commercialization. We also do not have any current contractual relationships for the manufacture of commercial supplies of any of our product candidates if and when they are approved. Our third-party manufacturers have made only a limited number of lots of our product candidates to date and have not made any commercial lots. The manufacturing processes for our product candidates have never been tested at commercial scale, and the process validation requirement has not yet been satisfied for any product candidate. These manufacturing processes and the facilities of our third-party manufacturers will be subject to inspection and approval by the FDA before we can commence the manufacture and sale of our product candidates, and thereafter on an ongoing basis. Some of our third-party manufacturers have never been inspected by the FDA and have not been through the FDA approval process for a commercial product. Some of our third-party manufacturers are subject to FDA inspection from time to time. Failure by these third-party manufacturers to pass such inspections and otherwise satisfactorily complete the FDA approval regimen with respect to our product candidates may result in regulatory actions such as the issuance of FDA Form 483 inspectional observations, warning letters or injunctions or the loss of operating licenses. Based on the severity of the regulatory action, our clinical or commercial supply of our product candidates could be interrupted or limited, which could have a material adverse effect on our business.

With respect to commercial production of our product candidates in the future, we plan on outsourcing production of the active pharmaceutical ingredients and final product manufacturing if and when approved for marketing by the applicable regulatory authorities. This process is difficult and time consuming and we can give no assurance that we will enter commercial supply agreements with any contract manufacturers on favorable terms or at all.

Reliance on third-party manufacturers entails risks, including:

- manufacturing delays if our third-party manufacturers give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of their agreements with us;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us;
- the possible breach of the manufacturing agreement by the third party;
- product loss due to contamination, equipment failure or improper installation or operation of equipment or operator error;
- the failure of the third-party manufacturer to comply with applicable regulatory requirements; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

Our manufacturers may not perform as agreed or may not remain in the contract manufacturing business. In the event of a natural disaster, business failure, strike or other difficulty, we may be unable to replace a third-party manufacturer in a timely manner and the production of our product candidates and potential products could be interrupted, resulting in delays and additional costs. We may also have to incur other charges and expenses for products that fail to meet specifications and undertake remediation efforts.

If third-party manufacturers fail to comply with manufacturing regulations, our financial results and financial condition will be adversely affected.

Before a third party can begin the commercial manufacturing of our product candidates and potential products, their manufacturing facilities, processes and quality systems must be in compliance with applicable regulations. Due to the complexity of the processes used to manufacture pharmaceutical products and product candidates, any potential third-party manufacturer may be unable to initially pass federal, state or international regulatory inspections in a cost effective manner. If contract manufacturers fail to pass such inspection, our commercial supply of drug substance will be significantly delayed and may result in significant additional costs. In addition, pharmaceutical manufacturing facilities are continuously subject to inspection by the FDA and comparable non-U.S. regulatory authorities, before and after product approval, and must comply with cGMP. Our contract manufacturers may encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. In addition, contract manufacturers' failure to achieve and maintain high manufacturing standards in accordance with applicable regulatory requirements, or the incidence of manufacturing errors, could result in patient injury, product liability claims, product shortages, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could seriously harm our business. If a third-party manufacturer with whom we contract is unable to comply with manufacturing regulations, we may also be subject to fines, unanticipated compliance expenses, recall or seizure of our products, product liability claims, total or partial suspension of production and/or enforcement actions, including injunctions, and criminal or civil prosecution. These possible sanctions could materially adversely affect our financial results and financial condition.

Furthermore, changes in the manufacturing process or procedure, including a change in the location where the product is manufactured or a change of a third-party manufacturer, will require prior FDA review and/or approval of the manufacturing process and procedures in accordance with the FDA's regulations, or comparable foreign requirements. This review may be costly and time consuming and could delay or prevent us from conducting our clinical trials or launching a product. The new facility will also be subject to pre-approval inspection. In addition, we have to demonstrate that the product made at the new facility is equivalent to the product made at the former facility by physical and chemical methods, which are costly and time consuming. It is also possible that the FDA may require clinical testing as a way to prove equivalency, which would result in additional costs and delay.

Any collaboration arrangement that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our current and future product candidates.

We plan to seek collaboration arrangements with pharmaceutical or biotechnology companies for the development or commercialization of our current and future product candidates outside of the United States. We will face, to the extent that we decide to enter into collaboration agreements, significant competition in seeking appropriate collaborators. Moreover, collaboration arrangements are complex and time consuming to negotiate, document and implement. We may not be successful in our efforts to establish and implement collaborations or other alternative arrangements should we choose to enter into such arrangements, and the terms of the arrangements may not be favorable to us. If and when we collaborate with a third party for development and commercialization of a product candidate, we can expect to relinquish some or all of the control over the future success of that product candidate

to the third party. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. To the extent such collaborators have programs that are competitive with our product candidates, they may decide to focus time and resources on development of those programs rather than our product candidates.

Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision making authority. Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

If we are not able to establish collaborations, we may have to alter our development and commercialization plans.

The development and potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such collaboration could be more attractive than the one with us for our product candidates. We may also be restricted under future license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

Risks Related to Intellectual Property

We may not be able to protect our proprietary technology in the marketplace.

We depend on our ability to protect our proprietary technology. We rely largely on trade secret and patent laws, and confidentiality, licensing and other agreements with employees and third parties, all of which offer only limited protection. Our success depends in large part on our ability and any future licensee's ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products. We believe we will continue to be able to obtain, through prosecution of our current pending patent applications, adequate patent protection for our proprietary drug technology. If we are compelled to spend significant time and money protecting or enforcing our patents or patent applications, designing around patents held by others or licensing or acquiring, potentially for large fees, patents or other proprietary rights held by others, our business and financial prospects may be harmed. If we are unable to effectively protect the intellectual property that we own, other companies may be able to offer the same or similar products for sale, which could materially adversely affect our competitive business position and harm our business prospects. Our patents may be challenged, narrowed, invalidated, or circumvented, which could limit our ability to stop competitors from marketing the same or similar products or limit the length of term of patent protection that we may have for our products.

The patent positions of pharmaceutical products are often complex and uncertain. The breadth of claims allowed in pharmaceutical patents in the United States and many jurisdictions outside of the United States is not consistent. For example, in many jurisdictions the support standards for pharmaceutical patents are becoming increasingly strict. Some countries prohibit method of treatment claims in patents. Changes in either the patent laws or interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property or create uncertainty. In addition, publication of information related to our current product candidates and potential products may prevent us from obtaining or enforcing patents relating to these product candidates and potential products, including, without limitation, composition-of-matter patents, which are generally believed to offer the strongest patent protection.

Our intellectual property consists of issued patents and pending patent applications related to our product candidates and other proprietary technology which cover compositions of matter, methods of use, combinations with other glaucoma products, formulations, polymorphs and the protection of the optic nerve. For *trabodenoson*, the composition patents are scheduled to expire in 2025 and 2026, in Europe and the United States, respectively. See "Business—Intellectual Property" included elsewhere in this prospectus for further information about our issued patents and patent applications.

Patents that we own or may license in the future do not necessarily ensure the protection of our product candidates for a number of reasons, including without limitation the following:

- we may not have been the first to make the inventions covered by our patents or pending patent applications;
- we may not have been the first to file patent applications for these inventions;
- any patents issued to us may not cover our products as ultimately developed;
- our pending patent applications may not result in issued patents, and even if they issue as patents, they may not provide us with any competitive advantages, or may be challenged and invalidated by third parties;
- our patents may not be broad or strong enough to prevent competition from other products that are identical or similar to our product candidates;
- there can be no assurance that the term of a patent can be extended under the provisions of patent term extension afforded by U.S. law or similar provisions in foreign countries, where available;

- our patents, and patents that we may obtain in the future, may not prevent generic entry into the U.S. market for our *trabodenoson* and other product candidates;
- we may be required to disclaim part of the term of one or more patents;
- there may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim;
- there may be patents issued to third parties that will affect our freedom to operate;
- if our patents are challenged, a court could determine that they are invalid or unenforceable;
- there might be significant changes in the laws that govern patentability, validity and infringement of our patents that adversely affects the scope of our patent rights;
- a court could determine that a competitor's technology or product does not infringe our patents;
- our patents could irretrievably lapse due to failure to pay fees or otherwise comply with regulations or could be subject to compulsory licensing; and
- we may fail to obtain patents covering important products and technologies in a timely fashion or at all.

In addition, on September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The United States Patent Office is currently developing regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act have not yet become effective. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act, in particular the first-to-file provision, and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

If we encounter delays in our development or clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced.

Our competitors may seek to invalidate our patents.

Our competitors may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may seek to market generic versions of any approved products by submitting Abbreviated New Drug Applications, or ANDAs, to the FDA in which our competitors claim that our patents are invalid, unenforceable and/or not infringed. Alternatively, our competitors may seek approval to market their own products similar to or otherwise competitive with our products. In these circumstances, we may need to defend and/or assert our patents, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid and/or unenforceable. We may also fail to identify patentable aspects of our research and development before it is too late to obtain patent protection. Even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

The issuance of a patent is not conclusive as to its inventorship, scope, ownership, priority, validity or enforceability. In that regard, third parties may challenge our patents in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized.

A significant portion of our intellectual property portfolio currently includes pending patent applications that have not yet issued as patents. If our pending patent applications fail to issue our business will be adversely affected.

Our commercial success will depend significantly on maintaining and expanding patent protection for our product candidates, as well as successfully defending our current and future patents against third-party challenges. As of June 30, 2014, we own at least 50 issued patents and have at least 30 pending patent applications in the United States and a number of foreign jurisdictions relating to our current product candidates and proprietary technology. See "Business—Intellectual Property" included elsewhere in this prospectus for further information about our issued patents and patent applications. Our intellectual property consists of patents and pending patent applications related to our product candidates and other proprietary technology which cover compositions of matter, methods of use, combinations with other glaucoma products, formulations, polymorphs and the protection of the optic nerve. For *trabodenoson*, the composition of matter patents are scheduled to expire in 2025 and 2026, in Europe and the United States, respectively.

There can be no assurance that our patent applications will issue as patents in the United States or foreign jurisdictions in which such applications are pending. Even if patents do issue on any of these applications, there can be no assurance that a third party will not challenge their validity or that we will obtain sufficient claim scope in those patents to prevent a third party from competing successfully with our products.

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

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to life sciences. To the extent we are able to obtain patents or other intellectual property rights in any foreign jurisdictions, it may be difficult for us to prevent infringement of our patents or misappropriation of these intellectual property rights. For example, some foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit.

Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate. In addition, changes in the law and legal decisions by courts in the United States and foreign countries may affect our ability to obtain adequate protection for our technology and the enforcement of intellectual property.

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

The United States Patent and Trademark Office, or the USPTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In this event, competitors might be able to enter the market earlier than would otherwise have been the case.

We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing our products.

Our commercial success depends significantly on our ability to operate without infringing the patents and other intellectual property rights of third parties. For example, there could be issued patents of which we are not aware that our product candidates or potential products infringe. There also could be patents that we believe we do not infringe, but that we may ultimately be found to infringe.

Moreover, patent applications are in some cases maintained in secrecy until patents are accepted or issued. The publication of discoveries in the scientific or patent literature frequently occurs substantially later than the date on which the underlying discoveries were made and patent applications were filed. Because patents can take many years to issue, there may be currently pending applications of which we are unaware that may later result in issued patents that our product candidates or potential products infringe. For example, pending applications may exist that claim or can be amended to claim subject matter that our product candidates or potential products infringe. Competitors may file continuing patent applications claiming priority to already issued patents in the form of continuation, divisional, or continuation-in-part applications, in order to maintain the pendency of a patent family and attempt to cover our product candidates.

Third parties may assert that we are employing their proprietary technology without authorization and may sue us for patent or other intellectual property infringement. These lawsuits are costly and could adversely affect our results of operations and divert the attention of managerial and scientific personnel. If we are sued for patent infringement, we would need to demonstrate that our product candidates, potential products or methods either do not infringe the claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity or unenforceability is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on us. In addition, we may not have sufficient resources to bring these actions to a successful conclusion. If a court holds that any third-party patents are valid, enforceable and cover our products or their use, the holders of any of these patents may be able to block our ability to commercialize our products unless we acquire or obtain a license under the applicable patents or until the patents expire. We may not be able to enter into licensing arrangements or make other arrangements at a reasonable cost or on reasonable terms. Any inability to secure licenses or alternative technology could result in delays in the introduction of our products or lead to prohibition of the manufacture or sale of products by us. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, in any such proceeding or litigation, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Any claims by third parties that we have misappropriated their confidential information or trade secrets could have a similar negative impact on our business. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations.

We may face claims of infringement, misappropriation or other violations of the rights of third-party intellectual property holders.

Pharmaceutical companies, biotechnology companies and academic institutions may compete with us in the commercialization of *trabodenoson* for use in ophthalmic indications and filing patent applications potentially relevant to our business. In order to contend with the strong possibility of third-party intellectual property conflicts, we periodically conduct freedom-to-operate studies, but such studies may not uncover all patents relevant to our business.

From time to time, we find it necessary or prudent to obtain licenses from third-party intellectual property holders. Where licenses are readily available at reasonable cost, such licenses are considered a normal cost of doing business. In other instances, however, we may use the results of freedom-to-operate studies to guide our early-stage research away from areas where we are likely to encounter obstacles in the form of third-party intellectual property. For example, where a third party holds relevant intellectual property and is a direct competitor, a license might not be available on commercially reasonable terms or available at all. We strive to identify potential third-party intellectual property issues in the early stages of research of our research programs, in order to minimize the cost and disruption of resolving such issues.

In spite of these efforts to avoid obstacles and disruptions arising from third-party intellectual property, it is impossible to establish with certainty that our products will be free of claims that we infringe, misappropriate or otherwise violate the rights of third-party intellectual property holders. Even with modern databases and online search engines, freedom-to-operate searches are imperfect and may fail to identify relevant patents and published applications. Even when a third-party patent is identified, we may conclude that we do not infringe the patent or that the patent is invalid. If the third-party patent owner disagrees with our conclusion and we continue with the business activity in question, patent litigation may result. We might decide to initiate litigation in an attempt to have a court declare the third-party patent invalid or non-infringed by our activity.

We may be subject to claims that we or our employees have misappropriated the intellectual property, including trade secrets, of a third party, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities, biotechnology companies or other pharmaceutical companies, including our competitors or potential competitors. Some of these employees, including each member of our senior management, executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we try to ensure that our employees do not use the intellectual property and other proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed such intellectual property, including trade secrets or other proprietary information. Litigation may be necessary to defend against these claims. We are not aware of any threatened or pending claims related to these matters or concerning the agreements with our senior management, but litigation may be necessary in the future to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such

claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and scientific personnel.

We may be unable to adequately prevent disclosure of trade secrets and other proprietary information.

We rely on trade secrets to protect our proprietary know-how and technological advances, especially where we have not filed a patent application or where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to protect our trade secrets and other proprietary information. However, any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets. Accordingly, these agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights. In addition, others may independently discover our trade secrets and proprietary information. Further, the FDA, as part of its Transparency Initiative, a proposal by the FDA to increase disclosure and make data more accessible to the public, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all. Failure to obtain or maintain trade secret protection could enable competitors to use our proprietary information to develop products that compete with our products or cause additional, material adverse effects upon our competitive business position and financial results.

Detecting the disclosure or misappropriation of a trade secret and enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

Any lawsuits relating to infringement of intellectual property rights brought by or against us will be costly and time consuming and may adversely impact the price of our common stock.

We may be required to initiate litigation to enforce or defend our intellectual property. These lawsuits can be very time consuming and costly. There is a substantial amount of litigation involving patent and other intellectual property rights in the pharmaceutical industry generally. Such litigation or proceedings could substantially increase our operating expenses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

In any infringement litigation, any award of monetary damages we receive may not be commercially valuable. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are resolved. Further, any claims we assert against a perceived infringer could provoke these parties to assert counterclaims against us alleging that we have infringed their patents. Some of our competitors may be able to sustain the costs of such litigation or proceedings

more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

In addition, our patents and patent applications could face other challenges, such as interference proceedings, opposition proceedings, re-examination proceedings, and other forms of post-grant review. In the United States, for example, post-grant review has recently been expanded. Any of these challenges, if successful, could result in the invalidation of, or in a narrowing of the scope of, any of our patents and patent applications subject to challenge. Any of these challenges, regardless of their success, would likely be time consuming and expensive to defend and resolve and would divert our management and scientific personnel's time and attention.

In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the market price of our common stock.

We will need to obtain FDA approval of any proposed product names, and any failure or delay associated with such approval may adversely affect our business.

Any name we intend to use for our product candidates will require approval from the FDA regardless of whether we have secured a formal trademark registration from the USPTO. The FDA typically conducts a review of proposed product names, including an evaluation of the potential for confusion with other product names. The FDA may also object to a product name if it believes the name inappropriately implies certain medical claims or contributes to an overstatement of efficacy. If the FDA objects to any of our proposed product names, we may be required to adopt an alternative name for our product candidates. If we adopt an alternative name, we would lose the benefit of our existing trademark applications for such product candidate and may be required to expend significant additional resources in an effort to identify a suitable product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. We may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our ability to commercialize our product candidates.

If we do not obtain additional protection under the Hatch-Waxman Amendments and similar foreign legislation extending the terms of our patents and obtaining data exclusivity for our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA regulatory approval for our product candidates, one or more of our U.S. patents may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. Patent term restorations, however, cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval by the FDA.

The application for patent term extension is subject to approval by the USPTO, in conjunction with the FDA. It takes at least six months to obtain approval of the application for patent term extension. We may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain earlier approval of competing products, and our ability to generate revenues could be materially adversely affected.

Risks Related to Our Business Operations and Industry

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

We are currently a small company with three employees as of July 31, 2014, and we outsource to consultants or other organizations substantially all of our operations, including accounting, finance, research and development and conduct of clinical trials. In order to commercialize our product candidates, we will need to substantially increase our operations. We plan to continue to build our compliance, financial and operating infrastructure to ensure the maintenance of a well-managed company. We expect to significantly expand our employment base when we reach the full commercial stages of our current product candidates' life cycle.

Future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, maintain and integrate additional employees. In addition, to meet our obligations as a public company, we will need to increase our general and administrative capabilities. Our management, personnel and systems currently in place may not be adequate to support this future growth. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to:

- manage our clinical trials and the regulatory process effectively;
- manage the manufacturing of product candidates and potential products for clinical and commercial use;
- integrate current and additional management, administrative, financial and sales and marketing personnel;
- develop a marketing and sales infrastructure;
- hire new personnel necessary to effectively commercialize our product candidates;
- develop our administrative, accounting and management information systems and controls; and
- hire and train additional qualified personnel.

Product candidates that we may acquire or develop in the future may be intended for patient populations that are large. In order to continue development and marketing of these product candidates, if approved, we would need to significantly expand our operations. Our staff, financial resources, systems, procedures or controls may be inadequate to support our operations and our management may be unable to manage successfully future market opportunities or our relationships with customers and other third parties. In particular, we will need to build out our finance, accounting and reporting infrastructure to meet our reporting obligations as a public company. Because we have never had this infrastructure, there may be increased risk that we will not be able to adequately meet these reporting obligations in a timely manner.

In addition, we may in the future decide to move our primary office into a new facility to address our business needs. This potential relocation could disrupt our operations, resulting in slower realization of efficiencies and capacity which could be associated with our use of a new office space.

We are a clinical-stage company and it may be difficult for you to evaluate the success of our business to date and to assess our future viability.

We are a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of therapies for glaucoma. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, conducting research and developing our product candidates. We have not yet demonstrated our ability to successfully complete a pivotal Phase 3 clinical trial, obtain regulatory approval of a product candidate, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful

product commercialization. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history and more experience with late stage development and commercialization of product candidates.

In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition from a company with a product development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We depend upon our key personnel and our ability to attract and retain employees.

Our future growth and success depend on our ability to recruit, retain, manage and motivate our employees. We are highly dependent on our senior management team and our scientific founders, as well as the other principal members of our management and scientific teams. Although we have formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time. The loss of the services of any member of our senior management or scientific team or the inability to hire or retain experienced management personnel could adversely affect our ability to execute our business plan and harm our operating results.

Because of the specialized scientific and managerial nature of our business, we rely heavily on our ability to attract and retain qualified scientific, technical and managerial personnel. In particular, the loss of David P. Southwell, our President and Chief Executive Officer, Rudolf A. Baumgartner, M.D., our Executive Vice President and Chief Medical Officer, William K. McVicar, Ph.D., our Executive Vice President and Chief Scientific Officer or Dale Ritter, our Vice President—Finance, could be detrimental to us if we cannot recruit suitable replacements in a timely manner. We do not currently carry “key person” insurance on the lives of members of executive management. The competition for qualified personnel in the pharmaceutical field is intense. Due to this intense competition, we may be unable to continue to attract and retain qualified personnel necessary for the development of our business or to recruit suitable replacement personnel. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

Upon the closing of this offering, we will become subject to the periodic reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the Securities and Exchange Commission, or SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

If we engage in acquisitions in the future, we will incur a variety of costs and we may never realize the anticipated benefits of such acquisitions.

We may attempt to acquire businesses, technologies, services, products or other product candidates in the future that we believe are a strategic fit with our business. We have no present

agreement regarding any material acquisitions. However, if we do undertake any acquisitions, the process of integrating an acquired business, technology, service, product candidates or potential products into our business may result in unforeseen operating difficulties and expenditures, including diversion of resources and management's attention from our core business. In addition, we may fail to retain key executives and employees of the companies we acquire, which may reduce the value of the acquisition or give rise to additional integration costs. Future acquisitions could result in additional issuances of equity securities that would dilute the ownership of existing stockholders. Future acquisitions could also result in the incurrence of debt, actual or contingent liabilities or the amortization of expenses related to other intangible assets, any of which could adversely affect our operating results. In addition, we may fail to realize the anticipated benefits of any acquisition.

Our business is affected by macroeconomic conditions.

Various macroeconomic factors could adversely affect our business and the results of our operations and financial condition, including changes in inflation, interest rates and foreign currency exchange rates and overall economic conditions and uncertainties, including those resulting from current and future conditions in the global financial markets. For instance, if inflation or other factors were to significantly increase our business costs, it may not be feasible to pass through price increases to patients. Interest rates, the liquidity of the credit markets and the volatility of the capital markets could also affect the value of our investments and our ability to liquidate our investments in order to fund our operations.

Interest rates and the ability to access credit markets could also adversely affect the ability of patients, payors and distributors to purchase, pay for and effectively distribute our products. Similarly, these macroeconomic factors could affect the ability of our potential future contract manufacturers, sole-source or single-source suppliers or licensees to remain in business or otherwise manufacture or supply product. Failure by any of them to remain in business could affect our ability to manufacture products.

If product liability lawsuits are successfully brought against us, our insurance may be inadequate and we may incur substantial liability.

We face an inherent risk of product liability claims as a result of the clinical testing of our product candidates. We will face an even greater risk if we commercially sell our product candidates or any other potential products that we develop. We maintain primary product liability insurance and excess product liability insurance with an aggregate limit of $10 million that cover our clinical trials and we plan to maintain insurance against product liability lawsuits for commercial sale of our product candidates. Historically, the potential liability associated with product liability lawsuits for pharmaceutical products has been unpredictable. Although we believe that our current insurance is a reasonable estimate of our potential liability and represents a commercially reasonable balancing of the level of coverage as compared to the cost of the insurance, we may be subject to claims in connection with our clinical trials and, in the future, commercial use of our product candidates, for which our insurance coverage may not be adequate, and the cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial.

For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated adverse effects. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend

ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

- reduced resources of our management to pursue our business strategy;
- decreased demand for our product candidates or potential products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- initiation of investigations by regulators;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- significant costs to defend resulting litigation;
- diversion of management and scientific resources from our business operations;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

We will need to increase our insurance coverage if our product candidates receive marketing approval and we begin selling them. However, the product liability insurance we will need to obtain in connection with the commercial sales of our product candidates, if and when they receive regulatory approval, may be unavailable in meaningful amounts or at a reasonable cost. In addition, insurance coverage is becoming increasingly expensive. If we are unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, if and when they obtain regulatory approval, which could materially adversely affect our business, financial condition, results of operations, cash flows and prospects.

Additionally, we do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, employment practices liability, auto, property, workers' compensation, products liability and directors' and officers' insurance. We do not know, however, if we will be able to maintain insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would materially adversely affect our financial position, cash flows and results of operations.

Business interruptions could delay us in the process of developing our products and could disrupt our sales.

Our headquarters is located in Lexington, Massachusetts. We are vulnerable to natural disasters, such as severe storms and other events that could disrupt our business operations. We do not carry insurance for natural disasters and we may not carry sufficient business interruption insurance to compensate us for losses that may occur. Any losses or damages we incur could have a material adverse effect on our business operations.

Our business and operations would suffer in the event of system failures.

Despite the implementation of security measures, our internal computer systems, and those of our CROs and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

Our employees, independent contractors, principal investigators, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading, which could significantly harm our business.

We are exposed to the risk of fraud or other misconduct by employees and independent contractors, such as principal investigators, consultants, commercial partners and vendors. Misconduct by these parties could include failures to comply with the regulations of the FDA and comparable non-U.S. regulatory authorities, provide accurate information to the FDA and comparable non-U.S. regulatory authorities, comply with fraud and abuse and other healthcare laws in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and other business arrangements in the healthcare industry are subject to extensive laws intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws may restrict or prohibit a wide range of business activities, including, but not limited to, research, manufacturing, distribution, pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We adopted a code of ethics, but it is not always possible to identify and deter employee and other third-party misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws. If any such actions are instituted against us resulting from such misconduct those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate.

We and our development partners, third-party manufacturers and suppliers use biological materials and may use hazardous materials, and any claims relating to improper handling, storage or disposal of these materials could be time consuming or costly.

We and our development partners, third-party manufacturer and suppliers may use hazardous materials, including chemicals and biological agents and compounds that could be dangerous to human health and safety or the environment. Our operations and the operations of our third-party manufacturers and suppliers also produce hazardous waste products. Federal, state and local laws and regulations govern the use, generation, manufacture, storage, handling and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive and current or future environmental laws and regulations may impair our product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

Risks Related to this Offering and Ownership of Our Common Stock

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

Prior to this offering, there has not been a public market for our common stock. Although we expect to list our common stock on NASDAQ, if an active trading market for our common stock does

not develop following this offering, you may not be able to sell your shares quickly or above the initial public offering price. The initial public offering price for the shares was determined by negotiations between us and representatives of the underwriters and may not be indicative of prices that will prevail in the trading market, and the value of our common stock may decrease from the initial public offering price.

The trading price of our common stock is likely to be volatile, and you can lose all or part of your investment. The following factors, in addition to other factors described in this "Risk Factors" section and elsewhere in this prospectus, may have a significant impact on the market price of our common stock:

- announcements of regulatory approval or a complete response letter, or specific label indications or patient populations for its use, or changes or delays in the regulatory review process;
- announcements of therapeutic innovations or new products by us or our competitors;
- adverse actions taken by regulatory agencies with respect to our clinical trials, manufacturing supply chain or sales and marketing activities;
- any adverse changes to our relationship with manufacturers or suppliers;
- the results of our testing and clinical trials;
- the results of our efforts to acquire or license additional product candidates;
- variations in the level of expenses related to our existing product candidates or preclinical and clinical development programs;
- any intellectual property infringement actions in which we may become involved;
- announcements concerning our competitors or the pharmaceutical industry in general;
- achievement of expected product sales and profitability;
- manufacture, supply or distribution shortages;
- actual or anticipated fluctuations in our quarterly or annual operating results;
- changes in financial estimates or recommendations by securities analysts;
- trading volume of our common stock;
- sales of our common stock by us, our executive officers and directors or our stockholders in the future;
- general economic and market conditions and overall fluctuations in the U.S. equity markets;
- changes in accounting principles; and
- the loss of any of our key scientific or management personnel.

In addition, the stock market, in general, and small pharmaceutical and biotechnology companies have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. Further, the current decline in the financial markets and related factors beyond our control may cause our stock price to decline rapidly and unexpectedly.

We may be subject to securities litigation, which is expensive and could divert management attention.

Our share price may be volatile, and in the past companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Litigation of this type could result in substantial costs and diversion of management's attention and resources, which could adversely impact our business. Any adverse determination in litigation could also subject us to significant liabilities.

Our existing principal stockholders, executive officers and directors own a significant percentage of our common stock and will be able to exert a significant control over matters submitted to our stockholders for approval.

After this offering, our officers and directors, and stockholders who own more than 5% of our outstanding common stock before this offering will, in the aggregate, beneficially own approximately % of our common stock (after giving effect to the conversion of all outstanding shares of our convertible preferred stock but assuming no exercise of the underwriters' option to purchase additional shares and no exercise of outstanding options or warrants).

This significant concentration of share ownership may adversely affect the trading price for our common stock because investors often perceive disadvantages in owning stock in companies with controlling stockholders. As a result, these stockholders, if they acted together, could significantly influence all matters requiring approval by our stockholders, including the election of directors and the approval of mergers or other business combination transactions. These stockholders may be able to determine all matters requiring stockholder approval. The interests of these stockholders may not always coincide with our interests or the interests of other stockholders. This may also prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock.

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

The initial public offering price is substantially higher than the net tangible book value per share of our common stock. Investors purchasing common stock in this offering will pay a price per share that substantially exceeds the net tangible book value of our common stock. As a result, investors purchasing common stock in this offering will incur immediate dilution of $ per share, based on the initial public offering price of $ per share and our pro forma net tangible book value as of June 30, 2014. In addition, investors purchasing common stock in this offering will contribute % of the total amount invested by stockholders since inception but will only own % of the shares of common stock outstanding.

In the past, we have issued options and warrants to acquire shares of our capital stock at prices significantly below the assumed initial public offering price. To the extent any outstanding options or warrants are ultimately exercised or we issue additional shares of common stock to the holders of exchangeable shares of our subsidiary, you will sustain further dilution. Further, because we will need to raise additional capital to fund our clinical development programs, we may in the future sell substantial amounts of common stock or securities convertible into or exchangeable for common stock. These future issuances of equity or equity-linked securities, together with the exercise of outstanding options and warrants and any additional shares issued in connection with acquisitions, if any, may result in further dilution to investors. For more information, see "Dilution" for a more detailed description of the dilution to new investors in the offering.

Sales of a substantial number of shares of our common stock in the public market by our existing stockholders could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. Substantially all of our existing stockholders are subject to lock-up agreements with the underwriters of this offering that restrict the stockholders' ability to transfer shares of our common stock for a period of 180 days after the date of this prospectus. After this offering, we will have outstanding shares of common stock based on the number of shares outstanding as of June 30, 2014. Subject to limitations,

approximately shares will become eligible for sale upon expiration of the lock-up period, as calculated and described in more detail in the section entitled “Shares Eligible for Future Sale.” In addition, shares issued or issuable upon exercise of options and warrants vested as of the expiration of the lock-up period will be eligible for sale at that time. Sales of stock by these stockholders could have a material adverse effect on the trading price of our common stock.

Moreover, after this offering, holders of an aggregate of shares of our common stock will have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. Registration of these shares under the Securities Act of 1933, as amended, or the Securities Act, would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by our affiliates as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

Our management will have broad discretion in the use of the net proceeds from this offering and may allocate the net proceeds from this offering in ways that you and other stockholders may not approve.

Our management will have broad discretion in the use of the net proceeds, including for any of the purposes described in the section entitled “Use of Proceeds,” and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. The failure of our management to use these funds effectively could have a material adverse effect on our business, cause the market price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in short-term, investment-grade, interest-bearing instruments and U.S. government securities. These investments may not yield a favorable return to our stockholders.

If securities or industry analysts do not publish or cease publishing research or reports about us, our business or our market, or if they adversely change their recommendations or publish negative reports regarding our business or our stock, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts may publish about us, our business, our market or our competitors. We do not have any control over these analysts and we cannot provide any assurance that analysts will cover us or provide favorable coverage. If any of the analysts who may cover us adversely change their recommendation regarding our stock, or provide more favorable relative recommendations about our competitors, our stock price could decline. If any analyst who may cover us were to cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Because we do not intend to declare cash dividends on our shares of common stock in the foreseeable future, stockholders must rely on appreciation of the value of our common stock for any return on their investment.

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends in the foreseeable future. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, we expect that only appreciation of the price of our common stock, if any, will provide a return to investors in this offering for the foreseeable future.

If we are unable to substantially utilize our net operating loss carryforward, our financial results will be adversely affected.

As of December 31, 2013, we had net operating losses of approximately $69.3 million, which may be utilized against future federal and state income taxes. In general, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating losses, or NOLs, to offset future taxable income. In general, an ownership change occurs if the aggregate stock ownership of certain stockholders (generally 5% stockholders, applying certain look-through and aggregation rules) increases by more than 50% over such stockholders' lowest percentage ownership during the testing period (generally three years). Purchases of our common stock in amounts greater than specified levels, which will be beyond our control, could create a limitation on our ability to utilize our NOLs for tax purposes in the future. Limitations imposed on our ability to utilize NOLs could cause U.S. federal and state income taxes to be paid earlier than would be paid if such limitations were not in effect and could cause such NOLs to expire unused, in each case reducing or eliminating the benefit of such NOLs. Furthermore, we may not be able to generate sufficient taxable income to utilize our NOLs before they expire. If any of these events occur, we may not derive some or all of the expected benefits from our NOLs. In addition, at the state level there may be periods during which the use of NOLs is suspended or otherwise limited, which would accelerate or may permanently increase state taxes owed.

The requirements associated with being a public company will require significant company resources and management attention.

Following this offering, we will become subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act of 2002, as amended, or the Sarbanes-Oxley Act, the listing requirements of the securities exchange on which our common stock is traded and other applicable securities rules and regulations. The Exchange Act requires that we file annual, quarterly and current reports with respect to our business and financial condition and maintain effective disclosure controls and procedures and internal control over financial reporting. In addition, subsequent rules implemented by the SEC and NASDAQ may also impose various additional requirements on public companies. As a result, we will incur additional legal, accounting and other expenses that we did not incur as a nonpublic company, particularly after we are no longer an "emerging growth company" as defined in the Jumpstart Our Business Startups Act, or JOBS Act. Further, the need to establish the corporate infrastructure demanded of a public company may divert management's attention from implementing our growth strategy. We have made, and will continue to make, changes to our corporate governance standards, disclosure controls and financial reporting and accounting systems to meet our reporting obligations. However, the measures we take may not be sufficient to satisfy our obligations as a public company, which could subject us to delisting of our common stock, fines, sanctions and other regulatory action and potentially civil litigation.

We will incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to compliance initiatives. Failure to build our finance infrastructure and improve our accounting systems and controls could impair our ability to comply with the financial reporting and internal controls requirements for publicly traded companies.

As a public company, we will operate in an increasingly challenging regulatory environment. Once we no longer qualify as an "emerging growth company" under the JOBS Act, we will be required to comply with the Sarbanes-Oxley Act and the related rules and regulations of the SEC, expanded disclosures, accelerated reporting requirements and more complex accounting rules. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability

insurance and we may be required to incur substantial costs to maintain the same or similar coverage. We estimate that we will annually incur approximately $1.5 million to $2.5 million in expenses to ensure compliance with these requirements.

Section 404(a) of the Sarbanes-Oxley Act requires annual management assessments of the effectiveness of our internal control over financial reporting, starting with the second annual report that we would expect to file with the SEC and we will be required to disclose material changes made in our internal controls and procedures on a quarterly basis. Company responsibilities required by the Sarbanes-Oxley Act include establishing corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud. However, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act until the later of the year following our first annual report required to be filed with the SEC or the date we are no longer an “emerging growth company” as defined in the JOBS Act, because we are taking advantage of the exemptions contained in the JOBS Act.

To build the infrastructure to allow us to assess the effectiveness of our internal control over financial reporting, we will need to hire additional accounting personnel and improve our accounting systems, disclosure policies, procedures and controls. We are currently in the process of:

- hiring additional accounting and financial staff with appropriate public company experience;
- initiating plans to establish an outsourced internal audit function;
- initiating plans to upgrade our computer systems, including hardware and software;
- establishing more robust policies and procedures; and
- enhancing internal controls and our financial statement review process.

If we are unsuccessful in building an appropriate accounting infrastructure, we may not be able to prepare and disclose, in a timely manner, our financial statements and other required disclosures, or comply with existing or new reporting requirements.

During the evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. We cannot assure you that there will not be material weaknesses in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness in our internal control over financial reporting, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by NASDAQ, the SEC and comparable non-U.S. regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

The recently enacted JOBS Act will allow us to postpone the date by which we must comply with some of the laws and regulations intended to protect investors and to reduce the amount of information we provide in our reports filed with the SEC, which could undermine investor confidence in our company and adversely affect the market price of our common stock.

For so long as we remain an "emerging growth company" as defined in the JOBS Act, we may take advantage of certain exemptions from various requirements that are applicable to public companies that are not "emerging growth companies" including:

- the provisions of Section 404(b) of the Sarbanes-Oxley Act requiring that our independent registered public accounting firm provide an attestation report on the effectiveness of our internal control over financial reporting;
- the "say on pay" provisions (requiring a non-binding stockholder vote to approve compensation of certain executive officers) and the "say on golden parachute" provisions (requiring a non-binding stockholder vote to approve golden parachute arrangements for certain executive officers in connection with mergers and certain other business combinations) of the Dodd-Frank Wall Street Reform and Consumer Protection Act, or Dodd-Frank Act, and some of the disclosure requirements of the Dodd-Frank Act relating to compensation of its chief executive officer;
- the requirement to provide detailed compensation discussion and analysis in proxy statements and reports filed under the Exchange Act, and instead provide a reduced level of disclosure concerning executive compensation; and
- any rules that may be adopted by the Public Company Accounting Oversight Board requiring mandatory audit firm rotation or a supplement to the auditor's report on the financial statements.

We may take advantage of these exemptions until we are no longer an "emerging growth company." We would cease to be an "emerging growth company" upon the earliest of: (i) the last day of the first fiscal year following the fifth anniversary of the closing of this offering; (ii) the last day of the first fiscal year in which our annual gross revenues are $1 billion or more; (iii) the date on which we have, during the previous three-year period, issued more than $1 billion in non-convertible debt securities; or (iv) as of the end of any fiscal year in which the market value of our common stock held by non-affiliates exceeded $700 million as of the end of the second quarter of that fiscal year.

Although we are still evaluating the JOBS Act, we currently intend to take advantage of some, but not all, of the reduced regulatory and reporting requirements that will be available to us so long as we qualify as an "emerging growth company." For example, we have irrevocably elected under Section 107 of the JOBS Act not to take advantage of the extension of time to comply with new or revised financial accounting standards available under Section 102(b) of the JOBS Act. Our independent registered public accounting firm will not be required to provide an attestation report on the effectiveness of our internal control over financial reporting so long as we qualify as an "emerging growth company," which may increase the risk that weaknesses or deficiencies in our internal control over financial reporting go undetected. Likewise, so long as we qualify as an "emerging growth company," we may elect not to provide you with certain information, including certain financial information and certain information regarding compensation of our executive officers, that we would otherwise have been required to provide in filings we make with the SEC, which may make it more difficult for investors and securities analysts to evaluate our company. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock, and our stock price may be more volatile and may decline.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and our bylaws that will become effective prior to the closing of this offering, as well as provisions of the Delaware General Corporation Law, or DGCL, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions include:

- establishing a classified board of directors such that not all members of the board are elected at one time;
- allowing the authorized number of our directors to be changed only by resolution of our board of directors;
- limiting the removal of directors by the stockholders;
- authorizing the issuance of "blank check" preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders;
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings; and
- requiring the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal our bylaws.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. In addition, we are subject to Section 203 of the DGCL, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with an interested stockholder for a period of three years following the date on which the stockholder became an interested stockholder, unless such transactions are approved by our board of directors. This provision could have the effect of delaying or preventing a change of control, whether or not it is desired by or beneficial to our stockholders.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the sections entitled “Prospectus Summary,” “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Business,” contain forward-looking statements that are based on our management’s belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this prospectus include, but are not limited to, statements about:

- our anticipated cash needs and our estimates regarding our capital requirements and our needs for additional financing;
- federal, state, and non-U.S. regulatory requirements, including regulation of our current or any other future product candidates by the FDA;
- the success, timing and cost of our ongoing clinical trials and anticipated Phase 3 program for *trabodenoson* as a monotherapy and Phase 2 program for our FDC product candidate, including statements regarding the timing of initiation and completion of the trials;
- the timing of and our ability to submit regulatory filings with the FDA and to obtain and maintain FDA or other regulatory authority approval of, or other action with respect to, our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy, including with respect to our planned sales force in the United States and our partnering and collaboration efforts outside the United States;
- third-party payor reimbursement for our current product candidates or any other potential products;
- our expectations regarding the clinical efficacy of our product candidates and results of our clinical trials;
- the glaucoma patient market size and the rate and degree of market adoption of our product candidates by ophthalmologists, optometrists and patients;
- the timing, cost or other aspects of the commercial launch of our product candidates and potential future sales of our current product candidates or any other potential products;
- our expectations regarding licensing, acquisitions and strategic operations;
- the potential advantages of our product candidates;
- our expectations related to the use of proceeds from this offering;
- our competitors and their product candidates, including our expectations regarding those competing product candidates;
- our ability to protect and enforce our intellectual property rights, including our patented and trade secret protected proprietary rights in our product candidates; and
- anticipated trends and challenges in our business and the markets in which we operate.

We caution you that the foregoing list may not contain all of the forward-looking statements made in this prospectus.

In some cases, you can identify forward-looking statements by terminology such as “may,” “might,” “could,” “would,” “will,” “should,” “expect,” “intend,” “plan,” “anticipate,” “believe,” “estimate,” “predict,” “project,” “target,” “potential,” “continue” or the negative of these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that

may cause actual results to differ materially from current expectations include, among other things, those listed under “Risk Factors” and elsewhere in this prospectus. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this prospectus and the documents that we reference in this prospectus and have filed with the SEC as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this prospectus represent our views as of the date of this prospectus. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus.

INDUSTRY AND MARKET DATA

We obtained the industry and market data in this prospectus from our own internal estimates and research as well as from industry and general publications and research, surveys, studies and trials conducted by third parties. We believe and act as if the third party data contained herein, and the underlying economic assumptions relied upon therein, are generally reliable. Some data is also based on our good faith estimates, which are derived from management's knowledge of the industry and independent sources. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, while we believe the market opportunity information included in this prospectus is generally reliable and is based on reasonable assumptions, such data involves risks and uncertainties and are subject to change based on various factors, including those discussed under the heading "Risk Factors." These and other factors could cause our results to differ materially from those expressed in the estimates made by third parties and by us.

USE OF PROCEEDS

We estimate that the net proceeds to us from the sale of shares of common stock in this offering will be approximately $ million based upon an assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters' exercise their option to purchase additional shares in full, we estimate that our net proceeds will be approximately $ million, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

A $1.00 increase (decrease) in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the net proceeds to us from this offering by approximately $ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, an increase (decrease) of one million shares offered by us would increase (decrease) the net proceeds to us from this offering by approximately $ million, assuming the assumed initial public offering price remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. A share increase in the number of shares offered by us together with a concomitant $1.00 increase in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase the net proceeds to us from this offering by approximately $ million, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Conversely, a share decrease in the number of shares offered by us together with a concomitant $1.00 decrease in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would decrease the net proceeds to us from this offering by approximately $ million, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The principal purposes of this offering are to fund the continued testing of *trabodenoson* as a monotherapy and as a fixed-dose combination with *latanoprost* for the reduction of intraocular pressure, or IOP, fund the further increase of our financial flexibility, create a public market for our common stock, facilitate our access to the public equity markets and for general corporate purposes. We currently expect to use the net proceeds from this offering as follows:

- approximately $ million to $ million for direct clinical and non-clinical costs associated with the completion of both Phase 3 pivotal trials for *trabodenoson* monotherapy;
- approximately $ million to $ million for direct clinical and non-clinical costs associated with the development of a commercial formulation and the completion of a Phase 2 trial for our FDC product candidate; and
- the remainder for working capital and general corporate purposes.

Our expected use of net proceeds from this offering represents our current intentions based upon our present plans and business condition. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering or the amounts that we will actually spend on the uses set forth above. We may use a portion of the net proceeds of this offering for the acquisition or licensing, as the case may be, of additional technologies, other assets or businesses, or for other strategic investments or opportunities, although we have no current understandings, agreements or commitments to do so at this time.

The amount and timing of our actual expenditures will depend upon numerous factors, including the results of our continued testing of our product candidates and the other factors described under “Risk Factors” in this prospectus. Accordingly, our management will have flexibility in applying the net proceeds from this offering. An investor will not have the opportunity to evaluate the economic, financial or other information on which we base our decisions on how to use the proceeds.

Pending these uses, we intend to invest the net proceeds in high quality, investment grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government, or hold as cash.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay cash dividends will be made at the discretion of our board of directors. In addition, the terms of our outstanding indebtedness restrict our ability to pay cash dividends, and any future indebtedness that we may incur could preclude us from paying cash dividends. Investors should not purchase our common stock with the expectation of receiving cash dividends.

CAPITALIZATION

The following table sets forth our cash, cash equivalents and capitalization as of June 30, 2014:

- on an actual basis;
- on a pro forma basis to give effect to (i) the conversion of all outstanding shares of preferred stock, including all accrued and unpaid dividends thereon, into an aggregate of 30,450,953 shares of common stock upon the closing of this offering and (ii) the filing and effectiveness of our amended and restated certificate of incorporation, which will occur immediately prior to the closing of this offering; and
- on a pro forma as adjusted basis to give further effect to our sale in this offering of shares of common stock at an assumed initial public offering price of $ per share (the midpoint of the price range set forth on the cover page of this prospectus), after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

You should read the following table together with the sections titled “Selected Financial Data,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” “Description of Capital Stock” and the financial statements and related notes appearing elsewhere in this prospectus.

	As of June 30, 2014		
(in thousands, except share and per share amounts)	Actual (unaudited)	Pro Forma (unaudited)	Pro Forma As Adjusted (unaudited)
Cash and cash equivalents	$ 8,881	$ 8,881	$
Notes payable	$ 6,911	$ 6,911	
Series AA redeemable convertible preferred stock, $0.001 par value; 25,757,874 shares authorized and 23,204,783 shares issued and outstanding, actual; no shares authorized, issued and outstanding, pro forma and pro forma as adjusted	42,715	—	
Series X redeemable convertible preferred stock, $0.001 par value; 2,902,050 shares authorized and 1,892,320 shares issued and outstanding, actual; no shares authorized, issued and outstanding, pro forma and pro forma as adjusted	548	—	
Stockholders’ equity (deficit):			
Preferred stock, $0.001 par value; no shares authorized, issued and outstanding, actual; shares authorized, no shares issued and outstanding, pro forma and pro forma as adjusted	—	—	
Common stock, $0.01 par value; 32,857,171 shares authorized, 4,147,249 issued and 4,139,599 outstanding, actual; shares authorized, pro forma and pro forma as adjusted; 34,598,202 shares issued and 34,590,552 shares outstanding, pro forma; and shares issued and outstanding, pro forma as adjusted	41	346	
Additional paid-in capital	77,724	123,168	
Treasury stock, at cost, 7,650 shares	(176)	(176)	
Accumulated deficit	(123,505)	(123,505)	
Total stockholders’ equity (deficit)	(45,916)	(167)	
Total capitalization	$ 4,258	$ 6,744	$

The information above is illustrative only, and our capitalization following the completion of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing.

A $1.00 increase (decrease) in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the amount of cash and cash equivalents, total stockholders' equity (deficit) and total capitalization on a pro forma as adjusted basis by approximately $ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, an increase (decrease) of one million shares offered by us would increase (decrease) the amount of cash and cash equivalents, total stockholders' equity (deficit) and total capitalization on a pro forma as adjusted basis by approximately $ million, assuming the assumed initial public offering price remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. A share increase in the number of shares offered by us together with a concomitant $1.00 increase in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase each of cash and cash equivalents, total stockholders' equity (deficit) and total capitalization by approximately $ million, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Conversely, a share decrease in the number of shares offered by us together with a concomitant $1.00 decrease in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would decrease each of cash and cash equivalents, total stockholders' equity (deficit) and total capitalization by approximately $ million, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. The pro forma as adjusted information discussed above is illustrative only and will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing.

The actual, pro forma and pro forma as adjusted information set forth in the table above excludes (i) 48,137 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2014 with a weighted-average exercise price of $10.00 per share, (ii) 1,081,136 shares of common stock issuable upon the exercise of warrants outstanding, 852,230 of which have an exercise price of $0.01 per share, are exercisable for preferred stock prior to the closing of this offering and will terminate upon the closing of this offering, and 228,906 of which have an exercise price of $1.529 per share, are exercisable for preferred stock prior to the closing of this offering and are exercisable for common stock upon the closing of this offering; and (iii) shares of common stock reserved for future issuance under our 2014 Stock Option and Incentive Plan, or 2014 Plan.

DILUTION

If you invest in our common stock in this offering, your interest will be diluted to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering. We calculate net tangible book value per share by dividing the net tangible book value (tangible assets less total liabilities) by the number of outstanding shares of our common stock.

The historical net tangible book value of our common stock as of June 30, 2014 was $ million, or $ per share, based on 4,139,599 shares of common stock outstanding as of June 30, 2014, which excludes the conversion of all of our outstanding 25,097,103 shares of preferred stock, including all accrued and unpaid dividends thereon, into 30,450,953 shares of common stock immediately prior to the closing of this offering.

The pro forma net tangible book value of our common stock as of June 30, 2014 was $ million, or approximately $ per share of common stock, based on shares of our common stock outstanding, after giving effect to the conversion of all 25,097,103 outstanding shares of convertible preferred stock, including all accrued and unpaid dividends thereon, into 30,450,953 shares of common stock immediately prior to the closing of this offering.

After giving further effect to our sale of shares in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses, our pro forma as adjusted net tangible book value as of June 30, 2014 would be $, or $ per share. This represents an immediate increase in net tangible book value of $ per share to existing stockholders and an immediate dilution in net tangible book value of $ per share to purchasers of common stock in this offering, as illustrated in the following table:

Assumed initial public offering price per share		$
Historical net tangible book value per share	$	
Increase attributable to the pro forma transactions described above, before giving effect to this offering		
Pro forma net tangible book value per share as of June 30, 2014		
Increase in net tangible book value per share attributable to new investors		
Pro forma as adjusted net tangible book value per share at June 30, 2014 after giving effect to this offering		$
Dilution per share to new investors		$

A $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) the dilution to new investors by $ per share, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated expenses payable by us. Similarly, an increase (decrease) of one million shares offered by us would increase (decrease) the dilution to new investors by $ per share, assuming the assumed initial public offering price remains the same and after deducting estimated underwriting discounts and commissions and estimated expenses payable by us. A share increase in the number of shares offered by us together with a concomitant $1.00 increase in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase the dilution to new investors by approximately $ per share, after deducting estimated

underwriting discounts and commissions and estimated offering expenses payable by us. Conversely, a share decrease in the number of shares offered by us together with a concomitant $1.00 decrease in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would decrease the dilution to new investors by approximately $ per share, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

If the underwriters exercise their option to purchase additional shares in full, the pro forma as adjusted net tangible book value would be $ per share, and the dilution in pro forma as adjusted net tangible book value to investors in this offering would be $ per share. The following table summarizes, on a pro forma as adjusted basis as of June 30, 2014, the differences between the number of shares of common stock purchased from us, the total consideration and the average price per share paid by existing stockholders (giving effect to the conversion of all of our outstanding 25,097,103 shares of preferred stock, including all accrued and unpaid dividends thereon, into 30,450,953 shares of common stock prior to the closing of this offering) and by investors participating in this offering, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, at an assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus.

	Shares Purchased		Total Consideration		Average price / share
	Number	Percent	Amount	Percent	
Existing stockholders		%	$		$
New investors		%			
Total		%	$		$

The above discussion and tables are based on 4,139,599 shares of common stock issued and outstanding as of June 30, 2014 and also reflects the conversion of all outstanding shares of preferred stock, including all accrued and unpaid dividends thereon, into an aggregate of 30,450,953 shares of common stock immediately prior to the closing of this offering, and excludes:

- 48,137 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2014 at a weighted-average exercise price of $10.00 per share;
- 1,081,136 shares of common stock issuable upon the exercise of warrants outstanding, 852,230 of which have exercise price of $0.01 per share, are exercisable for preferred stock prior to the closing of this offering and will terminate upon the closing of this offering, and 228,906 of which have exercise price of $1.529 per share, are exercisable for preferred stock prior to the closing of this offering and are exercisable for common stock upon the closing of this offering; and
- shares of common stock reserved for future issuance under our 2014 Plan.

A $1.00 increase (decrease) in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the total consideration paid by new investors by approximately $ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

If the underwriters exercise their option to purchase additional shares in full, the number of shares of common stock held by existing stockholders will be reduced to % of the total number of shares of common stock to be outstanding after this offering, and the number of shares of common stock held by investors participating in this offering will be further increased to , or % of the total number of shares of common stock to be outstanding after this offering.

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

SELECTED FINANCIAL DATA

We derived the selected statements of operations data for the years ended December 31, 2012 and 2013 and the balance sheet data as of December 31, 2012 and 2013 from our audited financial statements appearing elsewhere in this prospectus. The selected statements of operations data for the six months ended June 30, 2013 and 2014 and the balance sheet data as of June 30, 2014 have been derived from our unaudited financial statements included elsewhere in this prospectus. These unaudited financial statements have been prepared on a basis consistent with our audited financial statements and, in the opinion of management, reflect all adjustments, consisting only of normal and recurring adjustments, necessary for a fair presentation of such financial data. You should read this data together with our financial statements and related notes appearing elsewhere in this prospectus and the information under the captions "Management's Discussion and Analysis of Financial Condition and Results of Operations." Our historical results are not necessarily indicative of our future results, and results for the six-month period ended June 30, 2014 are not necessarily indicative of the results to be expected for the year ending December 31, 2014 or any other interim periods or any future year or period.

	Year Ended December 31,		Six Months Ended June 30,	
	2012	2013	2013	2014
(in thousands, except share and per share data)			(unaudited)	
Statements of Operations Data:				
Operating expenses:				
Research and development	$ (3,542)	$ (5,330)	$ (2,304)	$ (3,412)
General and administrative	(2,307)	(1,324)	(1,021)	(494)
Loss from operations	(5,849)	(6,654)	(3,325)	(3,906)
Other income	4	3	–	–
Interest expense	(213)	(884)	(388)	(491)
Change in fair value of warrant liabilities	–	(81)	–	(598)
Net loss	$ (6,058)	$ (7,616)	$ (3,713)	$ (4,995)
Net loss per common share—basic and diluted	$ (1.98)	$ (2.48)	$ (1.18)	$ (1.70)
Weighted-average common shares outstanding—basic and diluted	4,124,880	4,131,863	4,124,880	4,139,599
Pro forma net loss per common share—basic and diluted (unaudited)		$ (0.35)		$ (0.21)
Pro forma weighted-average common shares outstanding—basic and diluted (unaudited)		29,413,014		33,796,398

	Year Ended December 31,		June 30,
	2012	2013	2014
(in thousands)			(unaudited)
Balance Sheet Data:			
Cash and cash equivalents	$ 1,372	$ 12,793	$ 8,881
Total assets	1,421	12,863	8,923
Convertible notes payable	2,713	–	–
Notes payable—current portion	–	1,410	2,899
Notes payable, net of current portion	–	5,395	4,012
Warrant liabilities	–	1,888	2,486
Total liabilities	3,789	10,525	11,576
Series AA redeemable convertible preferred stock	27,856	40,685	42,715
Accumulated deficit	(110,894)	(118,510)	(123,505)
Total stockholders' deficit	(30,930)	(38,895)	(45,916)

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our "Selected Financial Data" and our financial statements, related notes and other financial information included elsewhere in this prospectus. This discussion contains forward-looking statements that involve risks and uncertainties such as our plans, objectives, expectations and intentions. Our actual results could differ materially from those discussed in these forward looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those identified below and those discussed in "Risk Factors" included elsewhere in this prospectus.

Overview

We are a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of therapies for glaucoma. Glaucoma is a disease of the eye that is typically characterized by structural evidence of optic nerve damage, vision loss and consistently elevated intraocular pressure, or IOP. Our lead product candidate, *trabodenoson*, is a first-in-class selective adenosine mimetic that we rationally designed to lower IOP by restoring the eye's natural pressure control mechanism. Our product pipeline includes *trabodenoson* monotherapy delivered in an eye drop formulation, as well as a fixed-dose combination, or FDC, of *trabodenoson* with *latanoprost* given once-daily, or QD.

We are completing a Phase 2 trial of *trabodenoson* with *latanoprost* and expect results from this trial to be reported in the fourth quarter of 2014. We are planning an End-of-Phase 2 meeting with the U.S. Food and Drug Administration, or FDA, for *trabodenoson* in the first half of 2015. We expect to initiate a Phase 3 program for *trabodenoson* monotherapy in mid-2015, which will consist of two Phase 3 pivotal trials and a long-term safety study. Based on our estimates of the rate of patient enrollment and assuming commencement in mid-2015, we expect to report top-line data from the first of the two pivotal Phase 3 trials by late 2016 or early 2017, with a second pivotal trial being completed in 2017.

Since our inception on July 7, 1999, we have devoted substantially all of our resources to business planning, raising capital, product research and development, applying for and obtaining government and private grants, recruiting management, research and technical staff and other personnel, acquiring operating assets, and undertaking preclinical studies and clinical trials of our lead product candidates.

We have not completed development of any product candidate and we have therefore not generated any revenues from product sales. Prior to 2012, we generated revenues primarily from research grants received from governmental agencies and private companies as well as revenue earned under licensing and research collaboration contracts. All previously recognized revenue was unrelated to our current development efforts focused on our lead product candidate, *trabodenoson,* for the treatment of glaucoma and other diseases of the eye.

Historically, we have financed our operations principally through grants from government and private entities, private placements of preferred stock and issuances of convertible promissory notes and notes payable. Although it is difficult to predict our liquidity requirements, based upon our current operating plan, and assuming the successful closing of this offering, we believe we will have sufficient cash to meet our projected operating requirements for at least the next 18 months. See "Liquidity and Capital Resources."

Our net losses were $6.1 million and $7.6 million for the years ended December 31, 2012 and 2013, respectively. Our net losses were $3.7 million and $5.0 million for the six months ended June 30, 2013 and 2014, respectively. As of June 30, 2014, we had an accumulated deficit of $123.5 million.

Factors Affecting our Results of Operations

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we continue to invest in research and development and commence our Phase 3 program of *trabodenoson* in 2015. We also expect our expenses to increase as we complete formulation and manufacturing activities of our FDC product candidate and commence clinical trials in 2016. In addition, if we successfully launch *trabodenoson* as a monotherapy or any other product candidates, we expect to incur significant commercialization expenses related to sales, marketing, manufacturing and distribution of our products.

Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. We expect operating expenses to increase substantially to support an increased infrastructure and expanded operations. Accordingly, we may need to obtain additional funding in connection with our continuing operations. Adequate additional financing may not be available to us on acceptable terms, or at all. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts. We will need to generate significant revenues to achieve profitability, and we may never do so. As a result, we expect to incur significant expenses and increasing operating losses for the foreseeable future.

Financial Overview

Revenue

We have not generated any revenue from product sales since our inception and do not expect to generate any revenue from the sale of products in the near future. Our ability to generate revenues will depend heavily on the successful development, regulatory approval and commercialization of *trabodenoson* and any other future product candidates. Historically, we generated revenues primarily from research grants received from governmental agencies and private companies as well as revenue earned under licensing and research collaboration contracts that were unrelated to our current research and development programs. We have not generated any revenues after January 1, 2012.

Research and Development Expenses

Research and development expenses consist primarily of the costs associated with our research and development activities, conducting preclinical studies and clinical trials and activities related to regulatory filings. Our research and development expenses consist of:

- direct clinical and non-clinical expenses which include expenses incurred under agreements with contract research organizations, or CROs, contract manufacturing organizations and costs associated with preclinical activities and development activities and costs associated with regulatory activities;
- employee and consultant-related expenses, including salaries, benefits, travel and stock-based compensation expense for research and development personnel as well as consultants that conduct and support clinical trials and preclinical studies; and
- facilities and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies used in research and development activities.

We expense research and development costs as incurred. We record costs for some development activities, such as clinical trials, based on an evaluation of the progress to completion of specific tasks using data such as subject enrollment, clinical site activations or other information our vendors provide to us.

The following table summarizes our research and development expenses by type of activity for the years ended December 31, 2012 and 2013, and for the six months ended June 30, 2013 and 2014:

	Year Ended December 31,		Six Months Ended June 30,	
	2012	2013	2013	2014
(in thousands)			(unaudited)	
Trabodenoson—direct clinical and non-clinical	$1,988	$3,799	$1,319	$2,873
Personnel and other expenses:				
Employee and consultant-related expenses	1,341	1,339	873	468
Facility expenses	163	123	67	59
Other expenses	50	69	45	12
Total personnel and other expenses	1,554	1,531	985	539
Total research and development expenses	$3,542	$5,330	$2,304	$3,412

All research and development efforts and expenses for the years ended December 31, 2012 and 2013, and for the six months ended June 30, 2013 and 2014, relate to the development of *trabodenoson*. We do not track *trabodenoson*-related expenses by product candidate. All expenses related to *trabodenoson* as a monotherapy also benefit the FDC product candidate *trabodenoson* with *latanoprost*. We have expended approximately $42 million for external development costs related to *trabodenoson* from inception through June 30, 2014.

The process of conducting the necessary clinical research to obtain regulatory approval is costly and time consuming and the successful development of our product candidates is highly uncertain. Our future research and development expenses will depend on the clinical success of our product candidates, as well as ongoing assessments of the commercial potential of such product candidates. In addition, we cannot forecast with any degree of certainty which product candidates may be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements. We expect our research and development expenses to increase in future periods for the foreseeable future as we seek to complete development of our lead product candidate, *trabodenoson*, further develop our other product candidates and expand our research and development personnel to focus on these product candidate development activities.

The successful development and commercialization of our product candidates is highly uncertain. This is due to the numerous risks and uncertainties associated with product development and commercialization, including the uncertainty of:

- the scope, progress, outcome and costs of our clinical trials and other research and development activities;
- the efficacy and potential advantages of our product candidates compared to alternative treatments, including any standard of care;
- the market acceptance of our product candidates;
- obtaining, maintaining, defending and enforcing patent claims and other intellectual property rights;
- significant and changing government regulation; and
- the timing, receipt and terms of any marketing approvals.

A change in the outcome of any of these variables with respect to the development of *trabodenoson* or any other product candidate that we may develop could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the

FDA or another regulatory authority were to require us to conduct clinical trials or other testing beyond those that we currently contemplate for the completion of clinical development of *trabodenoson* or any other product candidate that we may develop or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development of that product candidate.

General and Administrative Expenses

General and administrative expenses consist of salaries and related benefit costs, including stock-based compensation for administrative personnel. Other significant general and administrative expenses include professional fees for legal, patents, consulting, auditing and tax services as well as other direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies used in general and administrative activities. We anticipate that our general and administrative expenses will increase in future periods to support increases in our research and development activities and as a result of increased headcount (especially in our accounting and finance departments), increased stock-based compensation charges, expanded infrastructure, increased costs for insurance, and increased legal, compliance, accounting and investor and public relations expenses associated with being a public company.

Interest Expense

Interest expense consists primarily of interest on our existing notes payable, interest on convertible promissory notes, amortization of loan discounts as well as interest calculated based on the amortization of the beneficial conversion feature of the convertible promissory notes. We expect that our existing notes payable will remain outstanding after the closing of this offering, and therefore expect to continue to incur interest expense on these notes in accordance with the terms of the agreements.

Other Income (Expense), Net

Other income (expense), net, consists primarily of non-cash expense related to changes in the fair value of our warrant liabilities arising from the warrants to purchase shares of Series AA Preferred Stock described in Note 7 of our consolidated financial statements and appearing elsewhere in this prospectus, offset by other income which is primarily comprised of interest income.

Results of Operations

Comparison of the Six Months Ended June 30, 2013 and 2014

The following table summarizes the results of our operations for the six months ended June 30, 2014 and 2013:

(in thousands)	Six Months Ended June 30, 2013	2014	Increase (Decrease)
	(Unaudited)		
Operating expenses:			
Research and development	$(2,304)	$(3,412)	$ 1,108
General and administrative	(1,021)	(494)	(527)
Total operating expenses	(3,325)	(3,906)	581
Interest expense	(388)	(491)	103
Other income (expense), net	–	(598)	598
Net loss	$(3,713)	$(4,995)	$ 1,282

Research and Development Expenses

Research and development expenses increased by $1.1 million to $3.4 million for the six months ended June 30, 2014, as compared to $2.3 million for the six months ended June 30, 2013. The increase resulted primarily from higher CRO and other direct clinical trial expenses related to the current Phase 2 trial of *trabodenoson* FDC, which began in August 2013. This increase was partially offset by decreases in expenses related to manufacturing of the active pharmaceutical ingredient needed to conduct the Phase 2 trial, as well as decreases in expenses related to consultants and stock-based compensation for research development personnel.

General and Administrative Expenses

General and administrative expenses decreased $0.5 million, to $0.5 million, for the six months ended June 30, 2014, as compared to $1.0 million for the six months ended June 30, 2013. The decrease resulted primarily from approximately $0.8 million of executive severance and payroll-related costs that are included in the six months ended June 30, 2013 and are related to the termination of our former CEO and CFO who were terminated in May 2013. Offsetting this amount is a reversal of approximately $0.3 million of stock based compensation also related to these terminations. The remainder of the change is due to reductions in patent and other professional services expenses offset by higher outside consultant expenses for financial and accounting support.

Interest Expense

Interest expense increased $0.1 million, to $0.5 million, for the six months ended June 30, 2014, as compared to $0.4 million for the six months ended June 30, 2013. The entire amount of interest expense, both coupon and discount amortization, for the six months ended June 30, 2014, was related to the notes payable that we issued to two financial entities in June 2013. The majority of interest expense for the six months ended June 30, 2013 was related to our convertible promissory notes which converted to equity in June 2013.

Other Income (Expense), Net

Other expense, net, increased $0.6 million, to $0.6 million, for the six months ended June 30, 2014, as compared to no other expense, net, for the six months ended June 30, 2013. The increase resulted from the non-cash expense related to changes in the fair value of our warrant liabilities arising from the warrants to purchase shares of Series AA Preferred Stock described in Note 7 of our consolidated financial statements appearing elsewhere in this prospectus.

Comparison of the Years Ended December 31, 2012 and 2013

The following table summarizes the results of our operations for the years ended December 31, 2013 and 2012:

	Year Ended December 31,		Increase (Decrease)
	2012	2013	
Operating expenses:			
Research and development	$(3,542)	$(5,330)	$ 1,788
General and administrative	(2,307)	(1,324)	(983)
Total operating expenses	(5,849)	(6,654)	805
Interest expense	(213)	(884)	671
Other income (expense), net	4	(78)	82
Net loss	$(6,058)	$(7,616)	$ 1,558

Research and Development Expenses

Research and development expenses increased by $1.8 million, to $5.3 million, for the year ended December 31, 2013, as compared to $3.5 million for the year ended December 31, 2012. The increase resulted entirely from higher CRO and other direct clinical expenses related to the current Phase 2 trial of *trabodenoson* FDC, which began in August 2013.

General and Administrative Expenses

General and administrative expenses decreased $1.0 million, to $1.3 million, for the year ended December 31, 2013, as compared to $2.3 million for the year ended December 31, 2012. Approximately $0.6 million of this decrease is due to lower stock-based compensation and included a reversal of $0.3 million in expenses related to the termination of our former CEO and CFO who were terminated in May 2013. The remaining decrease resulted primarily from lower patent, legal and consultant-related expenses offset by higher payroll-related expenses.

Interest Expense

Interest expense increased by $0.7 million, to $0.9 million, for the year ended December 31, 2013, as compared to $0.2 million for the year ended December 31, 2012. Approximately $0.5 million of the increase resulted from the interest expense related to our notes payable which we issued in June 2013. The remaining increase resulted from higher interest expense related to our convertible promissory notes which converted into equity in June 2013.

Other Income (Expense), Net

Net other income increased by $0.1 million and is the result of the non-cash income related to changes in the fair value of our warrant liabilities arising from the warrants to purchase shares of Series AA Preferred Stock described in Note 7 of our consolidated financial statements appearing elsewhere in this prospectus.

Liquidity and Capital Resources

Since inception, we have incurred accumulated net losses and negative cash flows from our operations. We incurred net losses of $5.0 million and $3.7 million for the six months ended June 30, 2014 and 2013, respectively. We incurred net losses of $7.6 million and $6.1 million for the years ended December 31, 2013 and 2012, respectively. Our operating activities used $6.5 million and $6.9 million of cash flows during the years ended December 2013 and 2012, respectively, and $3.9 million and $2.6 million for the six months ended June 30, 2014 and 2013, respectively. Historically, we have financed our operations principally through grants from government and private entities, private placements of preferred stock and issuances of convertible promissory notes and notes payable.

At June 30, 2014, we had cash and cash equivalents of $8.9 million. We invest our cash equivalents in operating or money market accounts in order to preserve principal.

On June 28, 2013, we entered into a notes payable agreement with two financial entities pursuant to which we issued a $3.5 million note to each lender and received net proceeds of $6.9 million. The notes bear interest at a rate of 11.0% per annum and mature on October 1, 2016. Payments for the initial 12 months of the term are interest only and thereafter require repayment of the principal balance, with interest, in 27 monthly installments. Under the terms of the notes payable agreements, we granted first priority liens and the loans are collateralized by our personal property, including cash and cash equivalents. The notes payable agreements also contain representations and warranties by us and the lenders, indemnification provisions in favor of the lenders, customary covenants (including limitations on other indebtedness, liens, acquisitions, investments and dividends, but no financial covenants), and events of default (including payment defaults, breaches of covenants following any applicable cure period, a material impairment in the perfection or priority of lenders' security interest or in the collateral, and events relating to bankruptcy or insolvency). The terms of our current indebtedness may limit our ability to incur additional debt and undertake strategic transactions that may be beneficial to holders of our common stock. As of June 30, 2014, the total principal balance owed under the notes payable was $7.0 million. In addition, we believe were in compliance with all covenants under the notes payable agreements as of June 30, 2014.

The following table summarizes our sources and uses of cash for each of the periods presented:

(in thousands)	Year Ended December 31, 2012	Year Ended December 31, 2013	Six Months Ended June 30, 2013	Six Months Ended June 30, 2014
			(unaudited)	
Cash used in operating activities	$(6,936)	$ (6,455)	$ (2,638)	$(3,912)
Cash used in investing activities	3	–	–	–
Cash provided by financing activities	2,500	17,876	16,590	–
Net increase (decrease) in cash and equivalents	$(4,433)	$11,421	$13,952	$(3,912)

Net cash used in operating activities

Net cash used in operating activities was $3.9 million for the six months ended June 30, 2014 and $2.6 million for the six months ended June 30, 2013. Net cash used in operating activities for the six months ended June 30, 2014 principally resulted from our net loss of $5.0 million partially offset by increases in non-cash expenses related to changes in the fair value of our warrant liabilities of $0.6 million and non-cash interest expenses of $0.1 million as well as increases in accounts payables and accrued expenses of $0.3 million. Net cash used in operating activities for the six months ended June 30, 2013 principally resulted from our net loss of $3.7 million partially offset by increases in accounts payable and accrued expenses of $0.8 million and net non-cash stock compensation and interest expenses of $0.2 million.

Net cash used in operating activities was $6.5 million for the year ended December 31, 2013 and $6.9 million for the year ended December 31, 2012. Net cash used in operating activities for the year ended December 31, 2013 principally resulted from our net loss of $7.6 million and decreases in accounts payable of $0.2 million partially offset by increases in accrued expenses of $0.9 million and net non-cash stock compensation and interest expenses of $0.3 million. Net cash used in operating activities for the year ended December 31, 2012 principally resulted from our net loss of $6.1 million and decreases in accrued expenses of $1.8 million partially offset by increases in non-cash stock compensation expenses of $0.5 million, non-cash interest expenses of $0.2 million and accounts payable of $0.2 million. Our net losses in all periods were the result of our significant operating expenses for research and development activities and general and administrative expenses.

Net cash used in investing activities

Net cash used in investing activities was not significant for all periods presented.

Net cash provided by financing activities

Net cash provided by financing activities was $0 for the six months ended June 30, 2014 and $16.6 million for the six months ended June 30, 2013. Net cash provided by financing activities for the six months ended June 30, 2013 resulted primarily from $8.7 million in net proceeds from the sale of our Series AA Preferred Stock, $6.9 million in net proceeds from our notes payable and $1.0 million in net proceeds from the sale of our convertible notes, which converted into Series AA Preferred Stock in June 2013.

Net cash provided by financing activities was $17.9 million for the year ended December 31, 2013 and $2.5 million for the year ended December 31, 2012. Net cash provided by financing activities for the year ended December 31, 2013 resulted primarily from $10.0 million in net cash proceeds from the sale of our Series AA Preferred Stock, $6.9 million in proceeds from our notes payable and $1.0 million in net proceeds from the sale of our convertible notes which converted into Series AA Preferred Stock in June 2013. Net cash provided by financing activities for the year ended December 31, 2012 principally resulted from the receipt of $2.5 million in proceeds from the sale of our convertible notes which converted into Series AA Preferred Stock in June 2013.

Operating Capital Requirements

To date, we have not generated any revenue from product sales. We do not know when, or if, we will generate any revenue from product sales. We do not expect to generate significant revenue from product sales unless and until we obtain regulatory approval of and commercialize one of our current or future product candidates. We anticipate that we will continue to generate losses for the foreseeable future and we expect the losses to increase as we continue the development of, and seek regulatory approvals for, our product candidates and begin to commercialize any approved products. Upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. In addition, subject to obtaining regulatory approval of any of our product candidates, we expect to incur significant commercialization expenses for product sales, marketing and manufacturing. Accordingly, we anticipate that we will need substantial additional funding in connection with our continuing operations.

Based on our current operating plan, we expect that our existing cash and cash equivalents as of June 30, 2014, together with anticipated net proceeds from this offering, will enable us to fund our operating expenses and capital expenditures requirements for at least the next 18 months. In that time, we expect that our expenses will increase substantially as we fund clinical development of *trabodenoson*, fund clinical development of our FDC product candidate, fund new and ongoing research and development activities, fund the additional expenses related to being a public company, working capital and other general corporate purposes. We have based our estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures necessary to complete the development and commercialization of our product candidates.

Our future capital requirements will depend on many factors, including:

- the costs, timing and outcome of regulatory reviews and approvals;
- the ability of our product candidates to progress through clinical development successfully;
- the initiation, progress, timing, costs and results of non-clinical studies and clinical trials for our other programs and potential products;
- the number and characteristics of the product candidates we pursue;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other products and technologies; and
- our ability to establish any future collaboration arrangements on favorable terms, if at all.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and may require the issuance of warrants, which could potentially dilute your ownership interest. If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or research programs or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when

needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

The following summarizes our significant contractual obligations as of December 31, 2013:

(in thousands)	Total	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years
Operating lease obligations(1)	$ 67	$ 54	$ 13	$ –	$ –
Notes payable(2)	8,319	2,148	6,171	–	–
Severance payments(3)	145	145	–	–	–
Total	$8,531	$ 2,347	$6,184	$ –	$ –

(1) Amounts represent our minimum lease obligations related to our corporate headquarters in Lexington, Massachusetts. The minimum lease payments in the table do not include related common area maintenance charges or real estate taxes, which costs are variable.
(2) Amounts represent principal, interest and termination payments on our notes payable.
(3) Amount represents severance payments owed to our former CEO.

We enter into contracts in the normal course of business with CROs and contract manufacturers to assist in the performance of our research and development activities and other services and products for operating purposes. To the extent that these contracts provide for termination on notice, and therefore are cancelable contracts, they are not included in the table of contractual obligations and commitments.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under SEC rules.

Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risks in the ordinary course of our business. These market risks are principally limited to interest rate fluctuations. We had cash and cash equivalents of $8.9 million at June 30, 2014, consisting primarily of funds in operating cash accounts. The primary objective of our investment activities is to preserve principal and liquidity while maximizing income without significantly increasing risk. We do not enter into investments for trading or speculative purposes. Due to the short-term nature of our investment portfolio, we do not believe an immediate 1.0% increase in interest rates would have a material effect on the fair market value of our portfolio, and accordingly we do not expect a sudden change in market interest rates to affect materially our operating results or cash flows.

Because our notes payable bear interest at a fixed rate, a change in interest rates would not impact the amount of interest we would pay on our indebtedness.

JOBS Act

Under Section 107(b) of the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, an “emerging growth company” can delay the adoption of new or revised accounting standards until such time as those standards would apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and, as a result, we will adopt new or revised accounting standards at the same time as other public companies that are not emerging growth companies. There are other

exemptions and reduced reporting requirements provided by the JOBS Act that we are currently evaluating. For example, as an emerging growth company, we are exempt from Sections 14A(a) and (b) of the Exchange Act which would otherwise require us to (i) submit certain executive compensation matters to stockholder advisory votes, such as "say-on-pay," "say-on-frequency" and "golden parachutes" and (ii) disclose certain executive compensation related items such as the correlation between executive compensation and performance and comparisons of our Chief Executive Officer's compensation to our median employee compensation. We also intend to rely on an exemption from the rule requiring us to provide an auditor's attestation report on our internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and the rule requiring us to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board, or PCAOB, regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis. We will continue to remain an "emerging growth company" until the earliest of the following: the last day of the fiscal year following the fifth anniversary of the date of the closing of this offering; the last day of the fiscal year in which our total annual gross revenue is equal to or more than $1 billion; the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

Critical Accounting Policies and Estimates

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to:

- CROs in connection with performing research and development services on our behalf;
- investigative sites or other providers in connection with clinical trials;
- vendors in connection with non-clinical development activities; and
- vendors related to product manufacturing, development and distribution of clinical supplies.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple CROs that conduct and manage non-clinical studies and clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed, enrollment of patients, number of sites activated and level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting expenses that are too high or too low in any particular period.

Fair Value Measurements

We are required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. Accounting Standard Codification, or ASC, Topic 820, Fair Value Measurements and Disclosures, establishes a hierarchy of inputs used when available. Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of our company. Unobservable inputs are inputs that reflect our assumptions about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances. The fair value hierarchy applies only to the valuation inputs used in determining the reported fair value of the investments and is not a measure of the investment credit quality. The three levels of the fair value hierarchy are described below:

- Level 1—Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that we have the ability to access at the measurement date;
- Level 2—Valuations based on quoted prices for similar assets or liabilities in markets that are not active or for which all significant inputs are observable, either directly or indirectly;
- Level 3—Valuations that require inputs that reflect our own assumptions that are both significant to the fair value measurement and unobservable.

To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by us in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Our material financial instruments at June 30, 2014 and 2013 and December 31, 2013 and 2012 consist primarily of cash and cash equivalents and preferred stock warrant liabilities. We have determined that only our stock purchase warrant liability would be Level 3 fair value. We account for our stock purchase warrants as liabilities based upon the characteristics and provisions of the underlying instruments. These liabilities were recorded at their fair value on the date of issuance and are re-measured on each subsequent balance sheet date, with fair value changes recognized as income (decreases in fair value) or expense (increases in fair value) in other income (expense), net in the consolidated statements of operations.

Stock-Based Compensation

We measure the cost of employee services received in exchange for an award of equity instruments based on the grant date fair value of the award. That cost is recognized on a straight-line basis over the period during which the employee is required to provide service in exchange for the award. The fair value of options on the date of grant is calculated using the Black-Scholes option pricing model based on key assumptions such as stock price, expected volatility and expected term. Our estimates of these assumptions are primarily based on third-party valuations, historical data, peer company data and judgment regarding future trends and factors.

We account for stock options issued to non-employees in accordance with the provisions of The Financial Accounting Standards Board, or FASB, ASC Subtopic 505-50, *Equity-Based Payments to Non-employees*, which requires valuing the stock options using the Black-Scholes option pricing model and re-measuring such stock options at their current fair value as they vest.

Significant Factors, Assumptions and Methodologies Used in Determining Fair Value

Determining the fair value of our preferred stock warrants and stock-based awards requires the use of subjective assumptions. In the absence of a publicly traded market for our securities, we conducted periodic valuations of our securities.

Valuation of Series AA Preferred Stock Warrants as of June 30, 2013, December 31, 2013 and June 30, 2014

In connection with our June 30, 2014 valuation and in preparation for this offering, we performed a retrospective valuation for June 9, 2010 (which coincides with our grants of restricted Series X preferred stock), June 30, 2013 (which closely coincides with the issuance of warrants to purchase our Series AA preferred stock), and December 31, 2013. The valuation methods employed and significant assumptions are described below.

We engaged consultants to perform market research at our direction in the second half of 2012. This research concluded that our current product candidates could be well-positioned to compete effectively with existing drug therapies. We also obtained script data for current ophthalmology-related products and research data for other public companies developing products similar to our product candidates.

A third-party valuation consultant was engaged to advise and assist us in connection with the valuations of our Series AA preferred stock warrants as of June 30, 2013, December 31, 2013 and June 30, 2014. Because our Series X preferred stock is entitled to a contingent liquidation preference which varies based on the total value of our equity, we were precluded from using a closed-form model, such as the Black-Scholes option pricing method, to value the Series AA preferred stock warrants. Therefore, we employed a Monte Carlo simulation methodology for all models used to determine the fair value of securities in our capital structure.

Our initial equity value, or EV, was determined by utilizing a risk-adjusted discounted cash flow model based upon the market research described above, which is an income approach and was corroborated with market data, coupled with a series of Monte Carlo simulations which projected various equity values under different possible liquidity events including (i) initial public offering, or IPO, (ii) merger and acquisition, or M&A, and (iii) stay-private, or SP, scenarios. The first two scenarios assume successful completion of our current Phase 2 clinical trial, while the third scenario considers unfavorable results.

Key assumptions underlying the discounted cash flow model are described below:

- Based on the research described above and the industry knowledge of our officers and consultants, we developed projections of market penetration, product selling prices and required infrastructure to estimate our future revenues and operating expenses to determine projected free cash flows from our two current product candidates containing *trabodenoson*, through patent expiration.
- *Probability of Success.* To determine the probability of success for the various phases of development required for submission in an NDA, we utilized the clinical trial success rates as published in certain reports.
- *Time to Liquidity*. For each valuation date, we assumed liquidity events occurring between December 31, 2014 and April 1, 2015.
- *Risk Free rates*. Risk free rates are based on published or imputed government treasury rates as of each valuation date.

- *Volatilities*. Volatilities were derived from historical data from guideline publicly traded comparable companies. We used volatilities of 75% to 80% for the June 30, 2013 valuation, 60% to 65% for December 31, 2013 and 2014.

The Monte Carlo-simulated total equity values were then allocated to each type of security using a current value (waterfall) method under each scenario and were then probability-adjusted using probability weights by scenario.

As of date:	IPO	M&A	SP
June 30, 2013	–%	20%	80%
December 31, 2013	5%	20%	75%
June 30, 2014	30%	20%	50%

Retrospective 2010 Valuation

We performed a retrospective valuation of our Series X preferred stock as of its issuance in June 2010 for the purpose of determining an appropriate amount to record as stock-based compensation related to this stock grant. A third-party valuation consultant was engaged to advise and assist us in connection with the valuation of our Series X preferred stock as of the June 9, 2010 grant date. We implied the value of the Series X preferred stock from the value of the Series AA preferred stock investment made on the same date. We examined the parameters surrounding the Series AA preferred stock and determined that it adequately represented an arm's length transaction which constituted a Level 2 input for purposes of valuing the Series X preferred stock under a market approach.

The equity value as of this retrospective valuation date was estimated using a Monte Carlo simulation that would result in a per share value for the Series AA preferred stock equal to the price paid in the transaction. The simulated total equity values were allocated to each share class using a current value (waterfall) allocation method. The determined value of the Series X preferred stock represented the mean of all outputs from each Monte Carlo simulation model.

The per share value of Series X preferred stock on a fully marketable basis was estimated at $0.63 as of June 2010. We applied a discount for lack of marketability of 35% to the value of Series X preferred stock which resulted in a fair value per share of Series X preferred stock on a non-marketable interest basis of $0.41. A protective put option pricing model was used to estimate the discount for lack of marketability in the aforementioned Series X preferred stock valuation.

Results of Valuation Models May Vary

Valuation models require the input of highly subjective assumptions. Because our shares have characteristics significantly different from that of publicly traded common stock and because changes in the subjective input assumptions can materially affect the fair value estimate, in management's opinion, the existing models do not necessarily provide a reliable, single measure of the fair value of our Series AA preferred stock or Series X preferred stock. The foregoing valuation methodologies are not the only valuation methodologies available and are not expected to be used to value our securities after this offering is complete. We cannot make complete assurances as to any particular valuation for our securities. Accordingly, investors are cautioned not to place undue reliance on the foregoing valuation methodologies as an indicator of future stock prices.

BUSINESS

Overview

We are a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of therapies for glaucoma. Glaucoma is a disease of the eye that is typically characterized by structural evidence of optic nerve damage, vision loss and consistently elevated intraocular pressure, or IOP. Our lead product candidate, *trabodenoson*, is a first-in-class selective adenosine mimetic that we rationally designed to lower IOP by restoring the eye's natural pressure control mechanism. We developed this molecule to selectively stimulate a particular adenosine subreceptor in the eye with the effect of augmenting the intrinsic function of the eye's trabecular meshwork, or TM. The TM regulates the pressure inside the eye and is also the main outflow path for the fluid inside of the eye that often builds up pressure in patients with glaucoma. We believe that by restoring the natural function of the TM and this outflow path, rather than changing the fundamental dynamics of pressure regulation in the eye, *trabodenoson*'s mechanism of action should result in a lower risk of unintended side effects and long term safety issues than other mechanisms of action. Additionally, *trabodenoson*'s unique mechanism of action in the TM should complement the activity of existing glaucoma therapies that exert their IOP-lowering effects on different parts of the in-flow and out-flow system of the eye.

Our product pipeline includes *trabodenoson* monotherapy delivered in an eye drop formulation, as well as a fixed-dose combination, or FDC, of *trabodenoson* with *latanoprost* given once-daily, or QD. Statistically significant results for the primary endpoint of our completed Phase 2 clinical trial indicate that *trabodenoson* monotherapy has IOP-lowering effects in line with the best existing therapies, with a favorable safety and tolerability profile at all doses tested.

We are completing a Phase 2 trial of *trabodenoson* with *latanoprost* and expect results from this trial to be reported in the fourth quarter of 2014. We are planning an End-of-Phase 2 meeting with the U.S. Food and Drug Administration, or FDA, for *trabodenoson* monotherapy in the first half of 2015. We expect to initiate a Phase 3 program for *trabodenoson* monotherapy in mid-2015, which will consist of two Phase 3 pivotal trials and a long-term safety study. Based on our estimates of the rate of patient enrollment and assuming commencement in mid-2015, we expect to report top-line data from the first of the two pivotal Phase 3 trials by late 2016 or early 2017, with a second pivotal trial being completed in 2017. If the primary objectives of our Phase 3 program are met, we plan to submit a New Drug Application, or NDA, to the FDA for marketing approval of *trabodenoson* for the treatment of glaucoma in the United States. We plan to submit a marketing authorization application, or MAA, in Europe after filing our NDA for approval of *trabodenoson* in the United States.

According to IMS Health sales of glaucoma drugs in 2013 were approximately $2.0 billion in the United States and $5.6 billion worldwide. According to the British Journal of Ophthalmology, there were an estimated 2.8 million Americans with glaucoma in 2010. Once glaucoma develops, it is a chronic condition that requires life-long treatment. Prostaglandin analogs, or PGAs, are the most widely prescribed drug class for glaucoma and include the most widely prescribed glaucoma drug, *latanoprost.* When PGA monotherapy is insufficient to control IOP or is poorly tolerated, non-PGA products, such as beta blockers, alpha agonists and carbonic anhydrase inhibitors, are generally used either as an add-on therapy to the PGA or as an alternative monotherapy. Both PGAs and non-PGAs can cause adverse effects in the eye. In addition, non-PGA drugs can have adverse effects in the rest of the body and have been shown to have poor tolerability profiles. As a result, we believe there is a significant unmet need for a treatment that effectively lowers IOP by restoring outflow and the natural pressure control by the TM, that has a favorable safety and tolerability profile, and that works effectively in combination with other treatments.

Additionally, no existing treatments offer the potential to directly treat the underlying cause of glaucoma associated vision loss: the death of retinal ganglion cells, or RGCs, the nerve tissue in the retina that relays the visual signal to the brain. We believe that a drug with the potential to make these cells more resilient to the stress caused by glaucoma would achieve broad market acceptance as the treatment preferred among patients and physicians.

We own worldwide rights to all indications for our current product candidates and have patents and pending patent applications related to the composition of matter, pharmaceutical compositions and methods of use for *trabodenoson*, certain of which extend to 2031 with respect to our issued patents and 2034 with respect to our pending patent applications, if issued. If *trabodenoson* receives marketing approval in the United States, we plan to commercialize it by establishing our own specialty sales force in the United States.

Our Strategy

Our goal is to become a leading biopharmaceutical company focused on the discovery, development and commercialization of novel therapies to treat glaucoma. The key elements of our strategy are as follows:

- ***Complete clinical development and seek marketing approval for our lead product candidate, trabodenoson monotherapy***. In 2012, we completed a Phase 2 trial of *trabodenoson* monotherapy, which demonstrated statistically significant IOP-lowering and a favorable safety profile. We are planning an End-of-Phase 2 meeting with the FDA in the first half of 2015 to discuss our Phase 3 program for *trabodenoson* monotherapy and to confirm the design and endpoints for the Phase 3 pivotal trials. Based on our estimates of the rate of patient enrollment and assuming commencement in mid-2015, we expect to have top-line data from the first of two pivotal trials in the program by late 2016 or early 2017. If the primary objectives of our Phase 3 program are met, we plan to submit an NDA to the FDA for marketing approval of *trabodenoson* monotherapy for the treatment of glaucoma in the United States. We plan to submit an MAA in Europe after filing our NDA for approval of *trabodenoson* monotherapy in the United States.
- ***Complete clinical development and seek marketing approval of a fixed-dose combination product that includes both trabodenoson and latanoprost***. As many as half of glaucoma patients, typically those with more severe disease, need to use two or more glaucoma drugs to sufficiently reduce their IOP. The initial treatment for glaucoma patients is usually the use of a prescription eye drop from the PGA drug class. However, as PGAs are often unable to lower IOP sufficiently to reach the patient's medically targeted level, non-PGA products are used either as an add-on therapy to the PGA or as an alternative monotherapy in place of PGAs. There are currently no FDC products approved for use in the United States that include a PGA. We intend to formulate and conduct clinical development in order to seek marketing approval for an FDC product that includes both *trabodenoson* and *latanoprost*, the best-selling PGA. We believe that the favorable safety and tolerability profile and complementary mechanism of action of *trabodenoson* could, if approved, make an FDC with *latanoprost* a highly effective, well-tolerated and more convenient QD regimen for treating glaucoma in patients who have a less functional TM and therefore need additional help lowering their IOP. We expect to report data from our Phase 2 trial to support further development of our FDC product in late 2014.
- ***Establish a specialty sales force to maximize the commercial potential of trabodenoson in the United States***. We have retained worldwide commercial rights to *trabodenoson*. If *trabodenoson* receives marketing approval in the United States, we plan to commercialize it by establishing a glaucoma-focused specialty sales force of approximately 150 people targeting ophthalmologists and optometrists throughout the United States. For markets outside the

United States, we intend to explore partnership opportunities through collaboration and licensing arrangements.

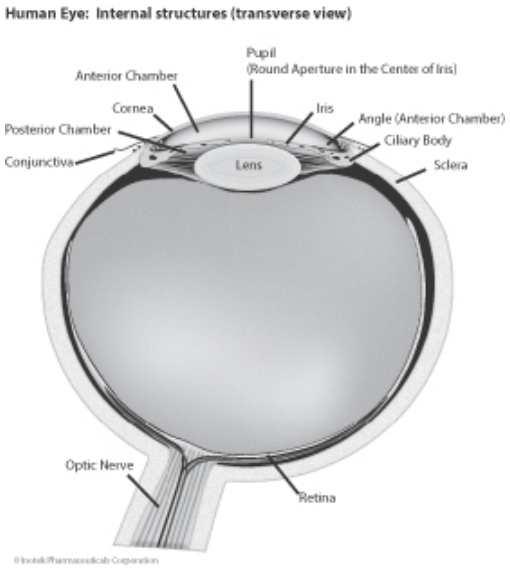
- ***Evaluate the potential of trabodenoson to slow the loss of vision associated with glaucoma or for additional ophthalmic indications.*** Based on an animal model that indicated *trabodenoson*'s potential to directly protect RGCs, the nerve tissue in the retina that relays the visual signal to the brain, we plan to conduct clinical trials to measure the rate of vision loss over time, rather than IOP control, in patients treated with *trabodenoson*. Should the results of these trials be positive, we plan to seek labeling indicative of *trabodenoson*'s potential to change the course of glaucoma-related vision loss, beyond that of IOP-lowering effect alone. In addition, this effect, if proven, could address the subset of glaucoma patients that do not have high IOPs, but still suffer from vision loss over time. We are also evaluating other potential indications where therapy with *trabodenoson* may be beneficial.

Glaucoma Overview

Glaucoma is a disease of the eye in which damage to the optic nerve leads to progressive, irreversible vision loss. Its characteristics can include structural evidence of optic nerve damage, vision loss and consistently elevated IOP.

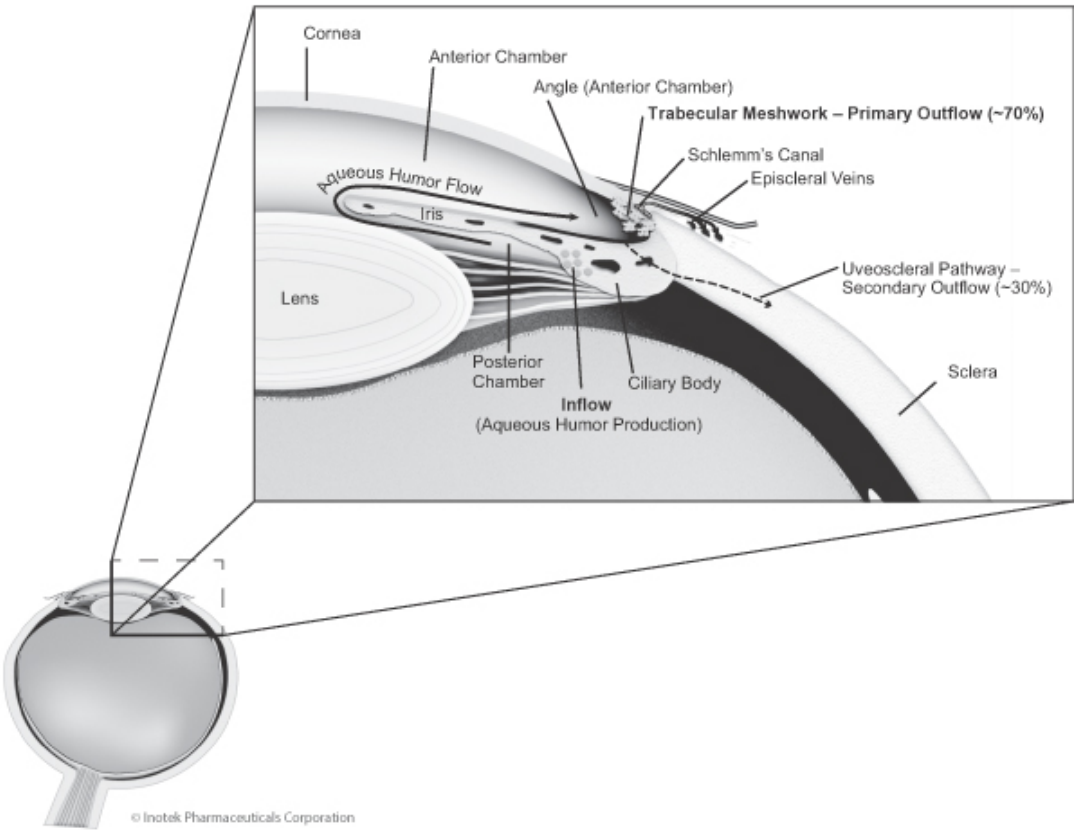
Physiology of the Eye

The eye is a fibrous sack which must stay "inflated" with a fluid that maintains the eye's form, known as aqueous humor, at the proper pressure in order to maintain its shape and effectively convey light to the retina where the light stimulus is then relayed to the brain and converted into a visual image. To maintain the eye's pressure—and therefore its shape—and as a means to provide nutrients to eye tissue, aqueous humor is constantly produced inside the eye by a tissue known as the ciliary body. The ciliary body sits just behind the iris, which is the colored part of the eye. Aqueous humor flows forward through a hole in the center of the iris, called the pupil, and down into the angle defined by the front of the iris and the back of the cornea, which is the clear covering on the front of the eye. This angle is the same angle referred to in Primary Open Angle Glaucoma, or POAG, the most common form of glaucoma. Below is a diagram depicting certain parts of the eye, including the ciliary body, iris and the angle defined by the front of the iris and the back of the cornea:



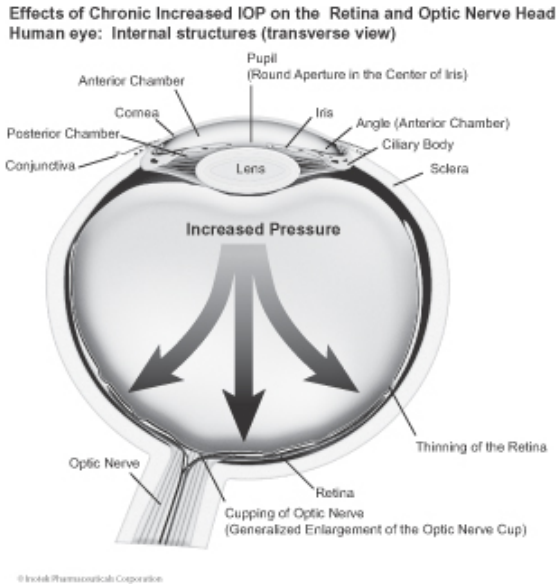
In this angle, around the outer rim of the iris, is the TM, a natural, pressure-regulating drain. It is here that in a healthy, well-functioning eye, approximately 70% of the aqueous humor exits and flows into a drainage canal known as Schlemm's canal, which empties back into the venous drainage system. The remaining approximately 30% of the aqueous humor leaves the eye through a secondary pathway called the uveoscleral pathway. The diagram below reflects the TM and the uveoscleral pathway, the two pathways for the aqueous humor to leave the eye.

Trabecular Meshwork and Aqueous Humor Dynamics



Development of High IOP and its Effects on Glaucoma

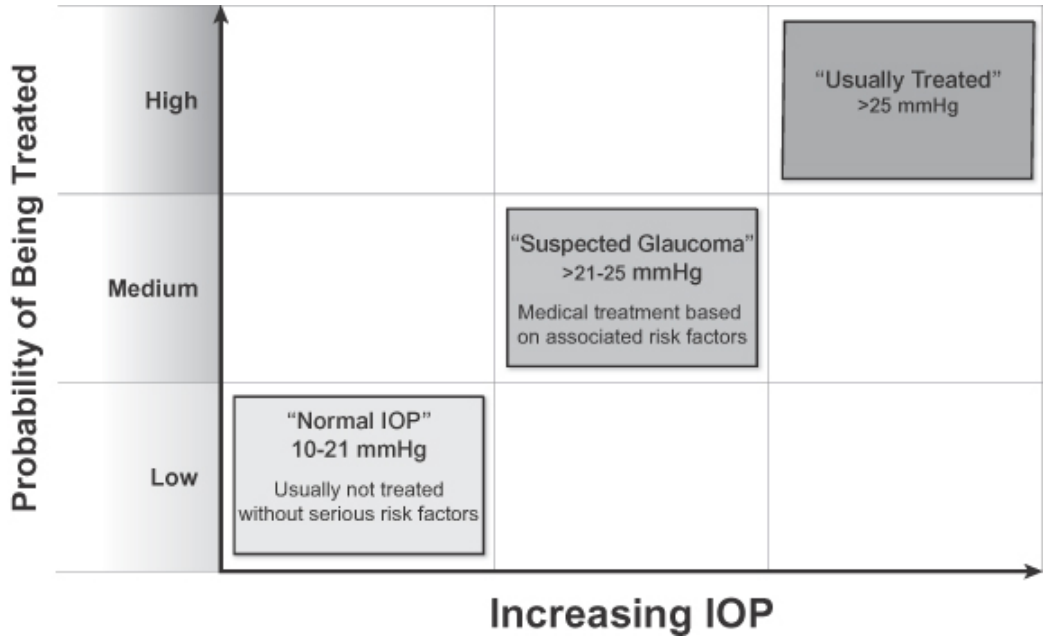
In a typical glaucoma patient, not enough aqueous humor exits the eye, creating excess pressure and squeezing the retina, the layer of tissue covering the inside of the back half of the eye that actually converts light into nerve impulses. For people to “see,” these impulses—the visual signal—must be relayed through the optic nerve back to the brain for processing. The cells in the retina require nutrients and oxygen that are delivered via blood vessels entering and exiting the eye through the same opening as the nerve fibers carrying the visual signal. However, when IOP is too high, it is more difficult to pump blood enriched in oxygen and nutrients into the retina. The diagram below reflects the anatomy of the eye and how elevated IOP can impair the nerve tissue in the retina and the optic nerve head.



The deprivation of blood supply to the retina may damage RGCs, the nerve tissue in the retina that relays the visual signal to the brain. These RGCs have long tails called axons that extend back to the brain to carry the visual image. In fact, the optic nerve is nothing more than a bundle of these axons extending to the vision processing center of the brain. When an RGC dies, one of the connections between the retina and the brain is lost, and like most cases when a nerve is damaged or cut—like in a spinal cord injury—there is no known way to repair the damage and, as a result, some portion of vision is permanently lost. Therefore, the root cause of vision loss in glaucoma is not high IOP per se, but the impact of high IOP on the retina, and specifically the RGCs.

Clinical Definition of Glaucoma

There are two key elements to the clinical definition of glaucoma: structural evidence of optic nerve damage and vision loss. Common risk factors include age, family history, corneal thickness and high IOP, commonly measured in millimeters of mercury, or mmHg. Currently, the only known way to treat glaucoma and slow the progression of vision loss is to reduce IOP. While treatment approaches are based on an assessment of the patient's risk factors for vision loss, elevated IOP is by far the best understood contributor to development of glaucoma. We believe that the general treatment patterns in the figure below, relative to a patient's IOP, are typical.



The Ocular Hypertension Treatment Study, or the OHTS Study, was a large, randomized academic trial published in 2002 that followed a total of 1,636 participants who initially had no evidence of glaucoma-related damage. The OHTS Study found that higher IOPs generally indicate a higher risk for progression to glaucoma. An IOP of 10 to 21 mmHg is generally considered in the normal range. Individuals with IOPs greater than 21 and up to 25 mmHg will often not be prescribed drug therapy unless they have evidence of both structural changes and some vision loss, or some combination of these and other risk factors for future vision loss. In fact, the United Kingdom's National Institute of Health and Care Excellence (NICE) Guidelines, for the treatment of suspected glaucoma (structural changes but without vision loss) plus elevated IOP, does not recommend treatment of eyes with corneal thickness of 555-590 nm and IOP of 25 mmHg or below. Drug treatment is much more common when patients have IOPs greater than 25 mmHg.

Glaucoma Market

According to the British Journal of Ophthalmology, there were an estimated 2.8 million Americans with glaucoma in 2010. According to the Archives of Ophthalmology, that number will reach approximately 3.4 million by 2020. Approximately 120,000 of these patients are suffering from blindness as a result of destruction to their optic nerve. Glaucoma can affect patients of all ages and ethnicities. However, according to the Archives of Ophthalmology, the prevalence rate (the proportion of people in the population that have glaucoma) increases with age. The most significant increases in

prevalence rates occur above 55 years of age. The prevalence in the population aged 65 years and younger is approximately twice that of the population 55 years or younger. Glaucoma is a chronic condition with no known cure and as a result patients are typically treated for the rest of their lives. Patients with glaucoma report decreased quality-of-life, difficulties with daily functioning, including driving, and are more likely to report falls and motor vehicle collisions.

According to IMS Health, in 2013, 31.2 million prescriptions were written for glaucoma medications in the United States. The majority of these prescriptions were for generic drugs, including *latanoprost* and *timolol*, which are the top two selling drugs for the treatment of glaucoma. Due to the lack of innovation in medications for glaucoma, most of the drugs used to treat glaucoma are generic drugs. Sales of glaucoma drugs in 2012 were approximately $1.9 billion in the United States and $5.5 billion worldwide. In 2013, sales of glaucoma drugs were approximately $2.0 billion in the United States and $5.6 billion worldwide, and IMS Health projects U.S. sales to be $3.1 billion in 2018, an increase of approximately 54% over 2013 sales.

Existing Glaucoma Treatments

The initial treatment for glaucoma patients is typically the use of a prescription eye drop from a class of drugs called PGAs. According to IMS Health, prescriptions for PGAs make up more than half of all prescriptions for glaucoma medications. The PGAs' primary mechanism of action for treating glaucoma is thought to be increasing fluid outflow through the uveoscleral pathway. A number of adverse effects are known to occur in all drugs in the PGA class and, as a result, these side effects are assumed to be associated with the mechanism of action. Most notable of these side effects is eye redness, or conjunctival hyperemia.

When PGAs are insufficient to control IOP or are poorly tolerated, non-PGA products are used either as an add-on therapy to the PGA or as an alternative monotherapy in place of a PGA. Non-PGAs can include a beta-blocker, an alpha (adrenergic) agonist or a carbonic anhydrase inhibitor alone. FDC products containing these non-PGAs are dominated by beta-blocker combinations, which can take the form of a beta-blocker combined with an alpha agonist (Combigan®), or a beta-blocker combined with a carbonic anhydrase inhibitor (Cosopt® or generic equivalent). Finally, there is a non-PGA combination (Simbrinza®) which consist solely of an alpha agonist and a carbonic anhydrase inhibitor. Non-PGA drugs generally have poorer tolerability in the eye than PGA drugs, and some have systemic adverse effects that limit the patient population in which they can be used safely. Moreover, their IOP-lowering effect is generally less than that of PGAs and the vast majority of non-PGAs are required to be dosed multiple times daily.

The existing classes of treatment available for glaucoma each have varying mechanisms of action, levels of IOP-lowering, side effects and other adverse effects, as described in the following table.

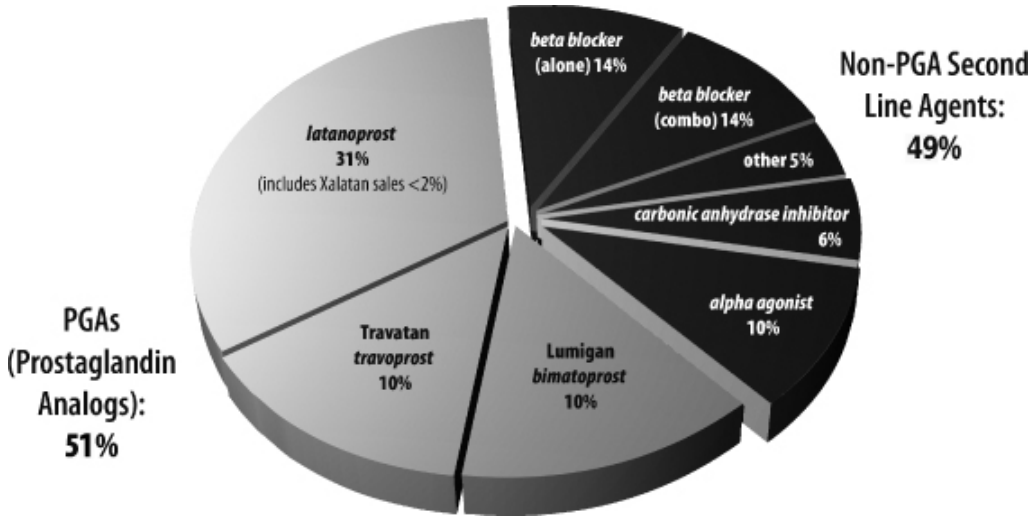
Summary of Existing Glaucoma Treatments:

Drug Classification *(Generic Names)*	Mechanism of Action*	IOP Reduction**	Known Side Effects*	Other Precautions, Warnings, Contraindications and Adverse Effects*
Prostaglandin analog *latanoprost* Travatan (*travoprost)* Lumigan *(bimatoprost)*	Increase uveoscleral and/or trabecular outflow	6-8 mmHg (25%-33%)	- Eye redness (conjunctival hyperemia) - Visual disturbances (blurred vision, loss of visual acuity) - Itching (pruritis) - Burning - Stinging - Eye pain - Darkening of the eyelids (periocular hyperpigmentation) - Permanent eye (iris) color change	- Macular edema - History of herpetic keratitis - Ocular edema
Beta-adrenergic antagonist, or beta-blocker *timolol*	Decrease aqueous production	N/A mmHg (20%-25%)	- Burning - Stinging - Eye lid swelling (Blepharitis) - Corneal inflammation (keratitis) - Itching (pruritis) - Eye pain - Dry eyes, foreign body sensation - Visual disturbances - Drooping eye lids (ptosis) - Swelling of retina (cystoid macular edema)	- Muscle weakness - Anaphylaxis - Severe respiratory and cardiac reactions - Contraindicated in bronchial asthma (or history of), severe chronic obstructive pulmonary disease, sinus bradycardia (slower heart rate), second or third degree atrioventricular block, overt cardiac failure, cardiogenic shock
Alpha-adrenergic agonist, or alpha agonist *brimonidine*	Decrease aqueous production; increase uveoscleral outflow	2-6 mmHg (20%-25%)	- Allergic conjunctivitis - Eye redness (conjunctival hyperemia) - Itchy eyes (eye pruritis)	- Severe cardiovascular disease - Depression - Cerebral or coronary insufficiency - High blood pressure (orthostatic hypertension) - Contraindicated in patients on monoamine oxidase inhibitor therapy
Carbonic anhydrase inhibitor *dorzolamide* *brinzolamide*	Decrease aqueous production	3-5 mmHg (15%-20%)	- Bitter taste - Burning - Stinging - Allergic conjunctivitis - Corneal inflammation (superficial punctate keratitis)	- Conjunctivitis - Eye lid reactions - Sulfonamide allergy

* According to FDA-approved labeling.

** mmHg, according to FDA-approved labeling; % from baseline, according to American Academy of Ophthalmology Glaucoma Panel.

The chart below illustrates the respective proportions of glaucoma prescriptions issued in 2013 by class, according to IMS Health.



Glaucoma Treatments Currently in Development.

We believe there are currently two leading classes of new drugs in clinical development for glaucoma: Rho kinase inhibitors and adenosine mimetics.

Certain Rho kinase inhibitors recently entered Phase 3 clinical trials and are the furthest along of the potential new glaucoma therapies. The most advanced of these, Aerie Pharmaceuticals, Inc.'s AR-13324, reported average IOP-lowering of 5.7 mmHg and 6.2 mmHg in two separate Phase 2 clinical trials in glaucoma patients after four weeks of treatment. Like with PGAs, conjunctival hyperemia has been reported with the Rho kinase inhibitor class.

Adenosine mimetics are compounds that mimic or simulate some of the actions or effects of adenosine, a naturally-occurring molecule with many, diverse biologic effects. There are four known subreceptors that are specific to adenosine: A1, A2a, A2b and A3. These subreceptors can cause many effects if stimulated. In the adenosine mimetic group, there are compounds targeting three different adenosine subreceptors: A1, A2a and A3. We believe that A1 selectivity is necessary for optimal IOP-lowering effect. To our knowledge, the two compounds being developed by other companies that were selective for the A2a subreceptor have been discontinued from clinical development for glaucoma. A third compound being developed that we believe targets both the A1 (IOP-lowering) and the A3 (IOP-increasing) subreceptors is still being studied. We believe that because this third compound is dosed orally, it is challenging to isolate its pharmacologic effects solely to the eye. We believe we are the only company to be developing an adenosine mimetic highly selective for the A1 subreceptor for ophthalmic indications.

Market Opportunity

Since 1996, there have been no new drug classes approved in the United States for glaucoma. As a result, there are persistent inadequacies in the tools that ophthalmologists use to manage patients with glaucoma. Thus, we believe there is a need for an innovative glaucoma treatment that offers:

- significant IOP-lowering;
- a favorable safety and tolerability profile;
- a novel mechanism of action that complements existing therapies; and
- convenient dosing.

Our Solution—*Trabodenoson*

Trabodenoson is a first-in-class selective adenosine mimetic that is designed to lower IOP with a mechanism of action that we believe augments the natural function of the TM. In addition, by enhancing a naturally occurring process to make the eye function more like that of a younger, healthier eye, rather than changing the fundamental dynamics of pressure regulation in the eye, we believe there is a lower risk of unintended side effects that could result in safety or tolerability issues in the long term. We believe *trabodenoson* enhances metabolic activity in the TM, which helps clear the pathway for the aqueous humor to flow out of the eye, thereby lowering IOP. We believe that *trabodenoson*'s mechanism of action improves the function of the eye, and that *trabodenoson* has the potential to be used as a monotherapy in place of current glaucoma treatments. In addition, we expect that *trabodenoson*'s purported mechanism of action in the TM should complement the activity of all currently-approved glaucoma drugs that work in other ways to lower IOP.

We believe the following elements of *trabodenoson*'s product profile will drive its adoption, if approved, in the glaucoma market:

- **Meaningful IOP-Lowering.** After four weeks of treatment in a Phase 2 clinical trial in glaucoma patients, *trabodenoson* (500 mcg) lowered IOP by an average of 6.5 mmHg from baseline. Moreover, IOP-lowering at week four was significantly better than IOP-lowering at week two. IOP-lowering for currently-approved glaucoma therapies, according to their FDA-approved labeling, ranges from 2-8 mmHg.
- **Favorable Safety Profile.** In three completed *trabodenoson* clinical trials over a wide range of doses, no patients have been withdrawn due to a *trabodenoson*-related side effect in the eye. In our most recently completed multiple-dose Phase 2 clinical trial, we did not observe side effects in the eye that would indicate a tolerability problem at any of the doses tested. Specifically, there was no change in the background rate of conjunctival hyperemia in the patient population when treatment with *trabodenoson* was initiated or continued for up to 28 days, even at the highest dose tested. No systemic effects of the drug have been identified, despite rigorous monitoring including cardiac and renal function, when administered as an eye drop. We believe this safety profile could be important in the potential for *trabodenoson* to become a preferred treatment alternative for patients that experience undesired side effects with existing therapies.
- **Unique, Complementary Mechanism of Action.** We believe that *trabodenoson*'s mechanism of action augments a naturally occurring process by clearing the path for aqueous humor outflow in the TM. We expect that this mechanism of action should complement all currently-approved glaucoma drugs which work in other ways to lower IOP, including by reducing aqueous humor production and increasing outflow through the uveoscleral pathway. This makes *trabodenoson*, with its favorable safety profile, a candidate to add to other glaucoma medications when a further reduction of IOP is desirable.

- **Convenient Dosing.** Current clinical data indicate that twice-a-day, or BID, dosing with *trabodenoson* is well tolerated and lowers IOP significantly. Moreover, after 28 days of BID dosing, the IOP-lowering effect persisted for an additional 24 hours after the last dose of medication, which suggests that *trabodenoson* could be dosed QD. We believe a QD dosing regimen minimizes the burden on patients to remember to take their medication, thus, we believe, potentially improving compliance with the therapy. If confirmed in our Phase 3 program, BID or QD dosing would make *trabodenoson* easier to use than most non-PGA products, and if QD dosing is confirmed and approved, *trabodenoson*'s dosing frequency would match the best-in-class PGAs, which would facilitate an FDC that could be dosed once a day.

We believe that *trabodenoson*'s efficacy, complementary mechanism of action, dosing profile and safety profile also make it well suited for use in an FDC with a PGA, which could be an effective and convenient option for patients currently using two or more glaucoma drugs to lower IOP.

Trabodenoson Discovery—Background

Adenosine is a naturally occurring molecule that has a broad array of biological effects. Its effects are mediated through activity at four known adenosine-specific subreceptors: A1, A2a, A2b and A3. These subreceptors are present throughout the body on the cells of different tissues, and at different concentrations. When adenosine binds and activates these different subreceptors, it can cause many diverse effects.

In 1995, a study was published in the Journal of Pharmacology and Experimental Therapeutics describing how adenosine mimetics can lower IOP by activating adenosine A1 subreceptors in rabbits. In 2001, an animal study published by the University of Pennsylvania School of Medicine confirmed that stimulation of A1 lowered IOP, but that stimulating A2a or A3 subreceptors increased IOP.

Our scientists began a rational deconstruction of this complex biology in order to isolate the protective activity of adenosine and to incorporate it into novel therapeutics. Beginning with the structure of adenosine, we created a series of molecules to bind with, and therefore induce the biological effects associated with stimulation of a single adenosine subreceptor. In this way, the undesired biological actions of native adenosine were systematically removed, one by one by eliminating the activity at non-target subreceptors. This rational drug design process relied heavily on our understanding of structure activity relationships, which relate the variation in the structure of the adenosine mimetics and their ability to bind and activate ideally just one adenosine subreceptor. Ultimately, a number of molecules emerged from these efforts with isolated and specialized activity, including some adenosine mimetics that only targeted the A1 subreceptor, leading to the discovery of *trabodenoson*.

The high affinity binding of *trabodenoson* to the A1 subreceptor is shown by the small Ki in the table below, and its selectivity for this IOP-lowering activity is indicated by much higher Ki's for A2a and A3 receptors where its binding is relatively weak.

Trabodenoson is a Potent and Selective A1 Adenosine Mimetic

Compound	A1 (Ki, nM)	A2a (Ki, nM)	A3 (Ki, nM)	Selectivity Ratios	
				A1/A3	A1/A2a
Trabodenoson	0.97	4,690	704	4,835x	725x

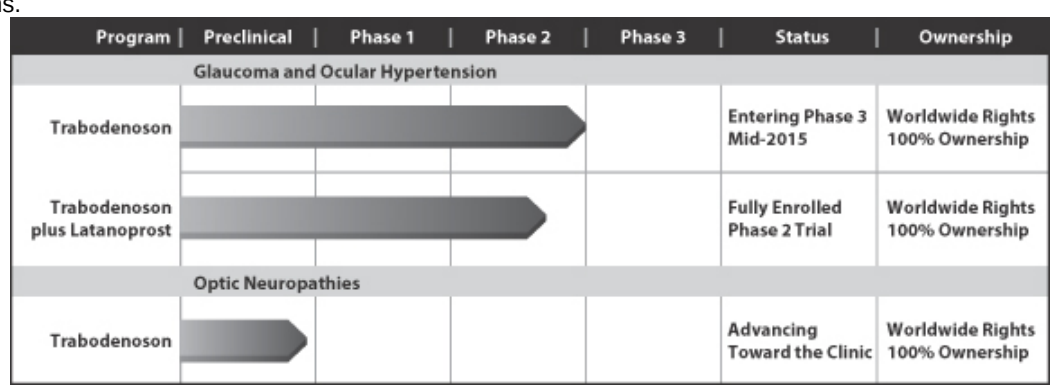
Trabodenoson's *key characteristics include:*

1. Potency—Ki in single-digit nM range (0.97nM);
2. High Selectivity—over A2a> 1000-fold and A3>500-fold;
3. Ease of Fat Solubility—allowing corneal penetration so it can reach the TM; and
4. A high compatibility with the often sensitive tissues in the front of the eye.

We believe that *trabodenoson* is the only adenosine mimetic with high selectivity for the single desired target of action, the A1 subreceptor, and that stimulation of this subreceptor in the TM effects a meaningful improvement in the metabolic activity in the TM that helps to clear the pathway for the aqueous humor to flow out of the eye, lowering IOP. This metabolic activity takes the form of an increase or up-regulation of proteases—such as Protease A or MMP-2—that digests and removes accumulated proteins that can block the healthy flow of the aqueous humor out of an eye with glaucoma. This metabolic activity is a naturally occurring or endogenous process that is enhanced by treatment with *trabodenoson*. We believe this process does not radically change the way the TM controls eye pressure, but rather restores the natural process of pressure control in the TM, which is different from other therapies that decrease aqueous humor production or increase the permeability of the eye to increase outflow.

Product Pipeline

Our product pipeline includes *trabodenoson*, as a monotherapy delivered in an eye drop formulation, as well as an FDC that includes *trabodenoson* plus *latanoprost* in an eye drop formulation, which we refer to as our FDC product candidate. We are also evaluating the potential for *trabodenoson* to directly target optic nerve neuropathies. The following table summarizes key information about our product development programs.



Trabodenoson

Our first product candidate, *trabodenoson*, is a monotherapy dosed in an eye drop. Our clinical trials have shown that *trabodenoson* has significant IOP-lowering effects, convenient dosing and also has a favorable safety profile when compared to the currently available glaucoma treatments, such as PGAs and non-PGAs.

Trabodenoson-Latanoprost Fixed-Dose Combination

As many as half of glaucoma patients, typically those with more severe disease, need to use two or more glaucoma drugs to sufficiently reduce their IOP. The available FDC products increase IOP-lowering but also have unpleasant tolerability challenges in the eye, as well as the adverse effects, safety warnings, precautions and contraindications that the two individually-dosed drugs carry in their FDA-approved package inserts. An FDC product containing a PGA plus a non-PGA has not yet been approved in the United States. We believe that none have gained FDA approval because the modest incremental benefit in IOP-lowering seen when a non-PGA is added to a PGA is too small in the context of the added side effects and clinical risks that come with the combined drugs. In contrast, we believe that an FDC containing a PGA and *trabodenoson* will benefit from significant incremental efficacy while adding very few side effects or clinical risks to the profile of the PGA alone. We believe such a product would be well received in the glaucoma market, especially for use in patients with higher IOPs that currently use two or more glaucoma drugs to lower IOP.

Our second product candidate is a combination of *trabodenoson* with a PGA, *latanoprost*, to create an FDC. While our FDC product candidate has not yet been formulated as an FDC or administered to humans, we expect that *trabodenoson* will not adversely affect the safety profile of *latanoprost*, or any other currently-approved PGA, because of its favorable safety and tolerability profile. We believe that *trabodenoson*'s mechanism for lowering IOP is likely to complement the mechanism of action of *latanoprost* and other PGAs, which work primarily on the secondary uveoscleral outflow, because *trabodenoson* is believed to act through the TM, the largest aqueous humor outflow path in the eye. In fact, our IOP-lowering studies in cynomolgus monkeys have shown that IOP-lowering is significantly better when the eye is treated with both *trabodenoson* and *latanoprost*, as compared to treatment with *latanoprost* alone. Moreover, *trabodenoson* appears to have a sufficiently long duration of action, which we believe may allow it to be effectively dosed QD in conjunction with *latanoprost* as an FDC. Assuming the *trabodenoson* safety profile remains favorable, a *trabodenoson-latanoprost* FDC therapy could present a much improved risk/benefit profile over other combinations of currently-approved PGAs and non-PGAs.

Trabodenoson for Optic Neuropathy

The neuroprotective potential of trabodenoson is supported by the basic biology of adenosine, which has shown that the stimulation of the A1 receptor can protect tissues of the central nervous system. While we have not yet conducted a formal program of studies to prove neuroprotection, we plan to study the potential of trabodenoson monotherapy and our FDC product candidate to slow the loss of vision significantly more than attributable to IOP lowering alone, either in glaucoma patients or in other rarer forms of optic nerve neuropathies.

Clinical Data and Development Strategy

Our planned Phase 3 program for *trabodenoson* as a monotherapy is expected to incorporate both the FDA-acceptable clinical endpoint of IOP, and to include studies with three months of treatment, both of which are well-known and accepted standards for pivotal trials for glaucoma. We are planning an End-of-Phase 2 meeting with the FDA in the first half of 2015 to discuss our Phase 3 program for *trabodenoson* monotherapy and to confirm the design and endpoints for the Phase 3 pivotal trials. *Timolol*, a non-PGA, will be used as the positive control in the Phase 3 pivotal trials due to its long

history of use as a glaucoma drug and the large amount of clinical data available on the drug, making it the comparator of choice in most recent Phase 3 trials in glaucoma. We plan to start our Phase 3 program for *trabodenoson* monotherapy in mid-2015, and we expect to report top-line data from the first pivotal trial in the program by late 2016 or early 2017, with the second pivotal trial being completed in 2017. If the primary objectives of our Phase 3 program are met, we plan to submit an NDA. We are planning to commence our Phase 3 program for the FDC of *trabodenoson* and *latanoprost* in 2017.

Clinical Results

Trabodenoson Phase 2 Tolerability, Safety and Efficacy in Glaucoma Patients

In 2012, we completed a successful Phase 2 dose-ranging clinical trial in 144 patients with ocular hypertension, or OHT (high IOP but no visual loss) or POAG, which demonstrated a clear dose response to *trabodenoson*. Statistically significant results for the primary endpoint of our Phase 2 clinical trials indicate that *trabodenoson* has IOP-lowering effects in line with the best existing therapies, with a favorable safety and tolerability profile at all doses tested. The trial was randomized, double-masked, placebo-controlled, and evaluated the efficacy, tolerability, safety, and pharmacokinetics of *trabodenoson* over two or four weeks of BID dosing with eye drops. Separate groups of patients received *trabodenoson* doses of 50, 100 or 200 mcg for 2 weeks, or 500 mcg for four weeks, and their IOP-lowering efficacy and safety data were compared to groups of patients dosed concurrently with placebo eye drops, also BID. To enter the trial, otherwise healthy patients had to have elevated IOPs (greater than or equal to 24 mmHg and less than or equal to 34 mmHg) when off of all glaucoma drugs, and a diagnosis of either OHT or POAG. POAG patients in this trial had elevated IOP due to dysfunctional pressure control, rather than due to angle closure which can also restrict the outflow path and increase IOP.

The primary efficacy endpoint was IOP (measured throughout the day, or diurnal IOP). The primary efficacy analysis calculated the reduction in diurnal IOP from the patients' IOP at the beginning of the study (recorded before active drug was administered at the study baseline). In the primary analysis, this IOP drop from baseline for each dose group (50, 100, 200 and 500 mcg) was then compared statistically to the IOP drop of a matched placebo group treated concurrently. A secondary efficacy analysis calculated the reduction from the individual patient's baseline IOP curve, collected on the day before they received their first dose of study drug. This baseline-corrected IOP drop was also compared statistically to that of the matched placebo group.

Safety evaluations included recording of withdrawals or terminations and adverse events. In each patient, the treated eye was evaluated at regular intervals with internal eye exams (including pupil dilation with slit lamp examination of the inside of the eye) and external eye examinations (of the outside surface of the eye, eye lids and surrounding tissue). Visual function was also assessed. Overall health was assessed by physical exam, vital signs (including heart rate and blood pressure), electrocardiograms, or ECGs, for heart function and analysis of urine and blood samples (clinical chemistry), and plasma samples were collected to analyze the pharmacokinetic parameters, such as the half-life of any drug detected in the systemic circulation.

Results

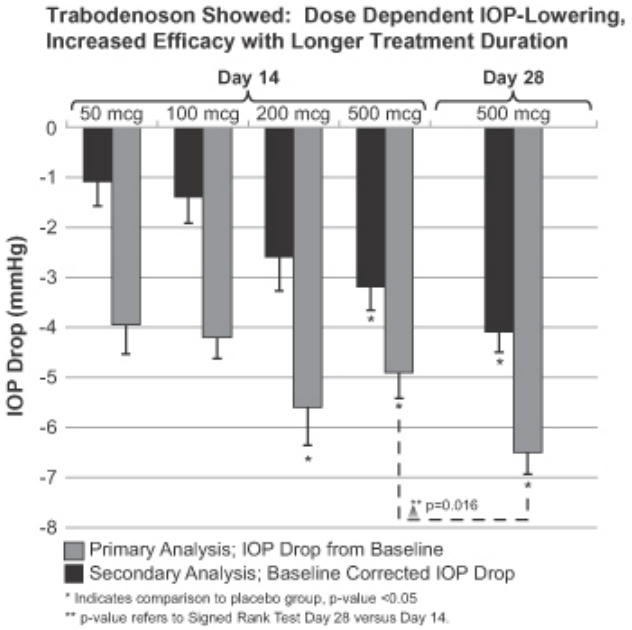
Patient Population: The characteristics of the patients in the dose groups were similar, including their ages, baseline IOPs, and diagnoses (OHT or POAG). The table below reflects information regarding the demographics of the patient populations that participated in the study, and shows that both diagnoses groups had similar baseline IOPs, and that groups treated with *trabodenoson* had characteristics that were similar to the placebo groups to which they were compared.

Baseline Demographics and IOP

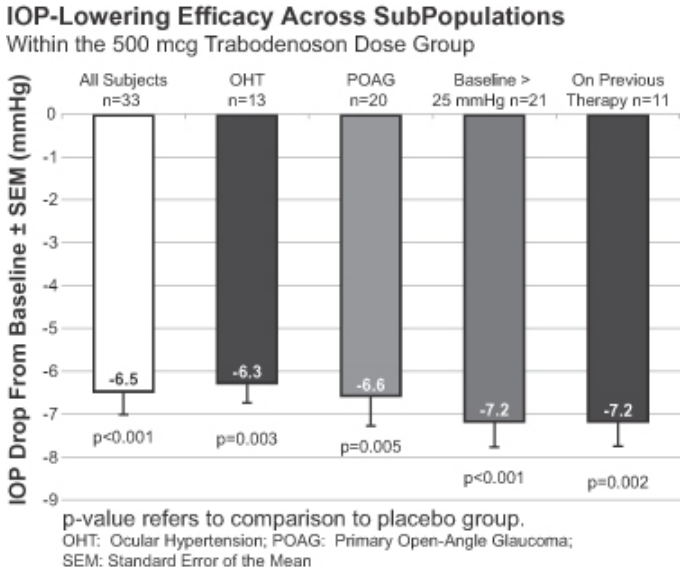
		Trabodenoson Dose				
	Placebo	50 mcg	100 mcg	200 mcg	500 mcg	Total Active
Mean Age	59	56.6	55.6	53.8	57.6	56.3
n	59	17	17	17	34	85
Baseline IOP (mmHg)	26.6	26.1	25.6	26.1	26.2	26
OHT n(%)	22(37.3)	6(35.3)	8(47.1)	6(35.3)	14(41.2)	34(40.0)
Baseline IOP (mmHg)	26.7	27.2	25	27.1	26.3	26.3
POAG n(%)	37(62.7)	11(64.7)	9(52.9)	11(64.7)	20(58.8)	51(60.0)
Baseline IOP (mmHg)	26.5	25.5	26.1	25.5	26.1	25.9

Efficacy

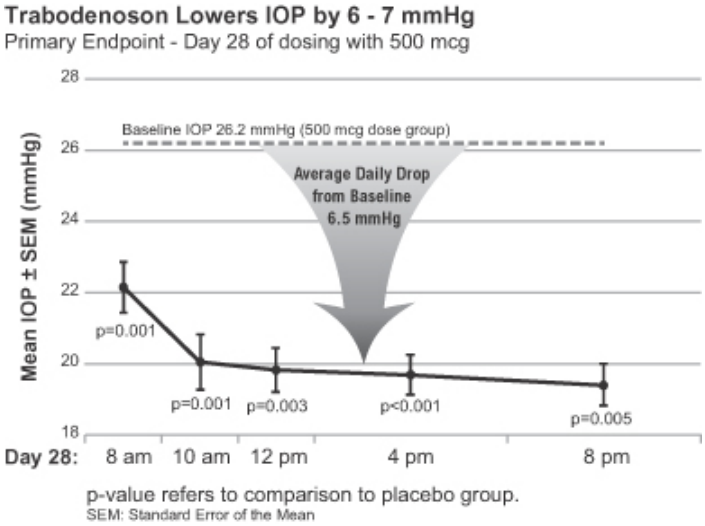
Both the 200 mcg dose (primary analysis Day 14) and the 500 mcg dose (primary and secondary analyses both at Day 14 and Day 28) met the primary endpoint demonstrating statistically significant improvements in IOP relative to the matched placebo ($p<0.05$ indicating a greater than 95% probability that the result was not a random event). Moreover, a clear increase in IOP-lowering efficacy was seen with increasing doses of *trabodenoson* (i.e. a dose response), and the most efficacious *trabodenoson* dose tested was the highest dose of 500 mcg. *Trabodenoson*'s primary efficacy endpoint (IOP drop from baseline) measured after four weeks of treatment (at Day 28) had improved significantly from the same endpoint when measured after two weeks of treatment (at Day 14). This improvement with treatment time was statistically significant ($p=0.016$). In the figure below, a clear trend for increasing IOP-lowering efficacy with increasing dose is evident. For the 500 mcg dose, the statistically significant increase in efficacy between Day 14 and Day 28 is illustrated on the right side of the figure.



The IOP-lowering at the highest and most efficacious dose (500 mcg) was evaluated in various patient sub-populations to gain a sense of the ability to generalize the results over a diverse patient population. The figure below compares the IOP drop from baseline (the primary endpoint analysis) for all patients (far left) to various sub-populations to the right of that. All of these patient subgroups responded to *trabodenoson*'s IOP-lowering effect.



When we rationally designed *trabodenoson*, our primary objective was to restore pressure regulation in eyes with high IOP, a risk factor for glaucoma. A healthy eye has a natural circadian rhythm that dictates a pattern of IOP over the day. We found that this pattern, or the shape of the IOP circadian rhythm curve throughout the day, is relatively unchanged by *trabodenoson* treatment, except that the overall IOP during the day is reduced by *trabodenoson* treatment as intended. We believe this indicates that the TM has been restored to an improved function resulting in a more normal average pressure, and that this normal daily IOP pattern indicates that the fundamental biology of pressure management in the eye has been preserved. The natural daily changes in IOP still exist, but at a significantly lower average pressure that we believe is less damaging to RGCs and the optic nerve. The figure below shows diurnal IOP and the primary endpoint for the trial at the highest dose tested at Day 28.



Furthermore, after 28 days of BID dosing, the IOP-lowering effect persisted for an additional 24 hours after the last dose of medication, which we believe may indicate the potential for *trabodenoson* to be dosed QD.

Safety and Tolerability

There were no serious adverse events or patients that withdrew due to safety findings that occurred once the drug was given. There were no signs of systemic safety issues in any of the non-ocular examinations, ECG evaluations or laboratory tests performed. Systemically, administration of *trabodenoson* eye drops was found to be well-tolerated. There were no changes noted from internal eye examinations or visual testing during drug treatment. The rate of conjunctival hyperemia in patients treated with *trabodenoson* was unchanged from the placebo run-in period (study baseline). There was no maximum tolerated dose determined because all doses tested were well-tolerated.

Trabodenoson Repeat-Dose Safety and Tolerability in Adult Healthy Volunteers

We conducted a randomized, double-masked, placebo-controlled, dose-escalation trial in healthy volunteers, aged 35-65, with the primary objective of characterizing the safety and tolerability profile of *trabodenoson* and identifying a maximum tolerated dose (a dose that was associated with limiting or intolerable side effects).

Ten subjects were assigned to each of seven consecutive cohorts (six to active *trabodenoson* and four to matched placebo). Cohorts 1 through 6 consisted of sequential, escalating doses (200, 400, 800, 1600, 2400 and 3200 mcg of *trabodenoson*) which were given topically to a single eye, BID, for 14 days. The 3200 mcg dose was the highest dose that could be administered to a single eye at one time

due to, among others, the limitations of the formulation. Cohort 7 included eight step-wise escalating doses of *trabodenoson*, given in both eyes. Doses given to this cohort ranged from 200-3200 mcg in a single eye and totaled 1800-6400 mcg for both eyes combined. Dose escalation to the next dose level proceeded only after masked review of the safety data from the preceding dose level.

Systemic safety assessments included: adverse events, other medications used, physical examinations, vital signs, clinical laboratory tests of blood and urine samples, extensive monitoring of cardiac function and health (12-lead ECG tracings, continuous cardiac monitoring and cardiac troponin concentrations), lung function testing (FEV_1), sleep (Karolinska Sleepiness Scale), kidney function and withdrawals or terminations. No systemic safety signals were found at any of the doses tested.

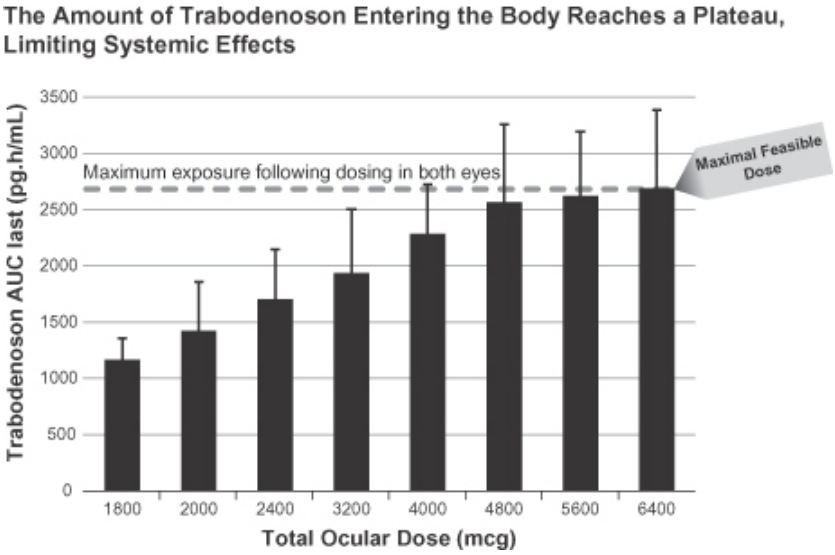
Ocular safety assessments included vision tests (visual acuity), IOP measurements, as well as internal and external eye examinations. No significant changes were seen in IOP measurements and examination of the periorbital area, eyelids, eyelashes, pupils, cornea, iris and sclera. The only ocular finding was short-lived, self-limited conjunctival hyperemia that was dose-related, usually mild in severity, decreased with continuing exposure, and was not accompanied by evidence that it was related to inflammation, such as persistent anterior chamber cells or flare. The incidence of clinically significant eye redness reported as an adverse event was extremely low (1 of 42) in subjects randomized to *trabodenoson*.

Early Terminations and Withdrawals

Three subjects randomized to placebo were terminated early from the study for reasons unrelated to the study drug. Only one subject assigned to active study drug was withdrawn. The study subject's laboratory tests revealed findings consistent with gallbladder disease (chronic cholecystitis), so the subject was withdrawn from the clinical trial (without unmasking the subject's treatment assignment) and referred for a surgical consult resulting in the subject having chronic gallbladder stones removed.

Pharmacokinetic Data

The pharmacokinetics data indicated that the exposure to *trabodenoson* generally increased in a dose-dependent manner. At the highest three doses, there were no apparent increases in systemic exposure with increasing dose. This plateau effect suggests that little additional drug is absorbed into systemic circulation following doses above 4800 mcg (2400 mcg per eye), as reflected in the figure below.



Conclusions

In conclusion, no safety or tolerability issues were identified in either the eye or the body as a whole. Due to the lack of clinically significant findings following in depth safety testing for systemic and ocular effects of *trabodenoson*, no maximum tolerated dose could be identified. Systemic exposure to *trabodenoson* appeared to be limited above ocular doses totaling 4800 mcg, indicating an apparent limitation to the amount of drug that can be delivered to the body by dosing in the eye.

Trabodenoson Monotherapy Tolerability, Safety and Efficacy

We conducted a Phase 1/2 multi-center, randomized, double-masked, placebo-controlled, dose-escalation trial in 70 adults with POAG and OHT with the primary objective of characterizing the safety and tolerability of increasing doses of a pilot formulation of *trabodenoson* monotherapy.

Subjects were sequentially assigned to one of seven consecutive cohorts (eight to active *trabodenoson* and four to matched placebo); consisting of sequential, escalating single-doses of 2.5, 7.5, 20, 60, 180, 350 or 700 mcg of *trabodenoson* given topically to a single study eye.

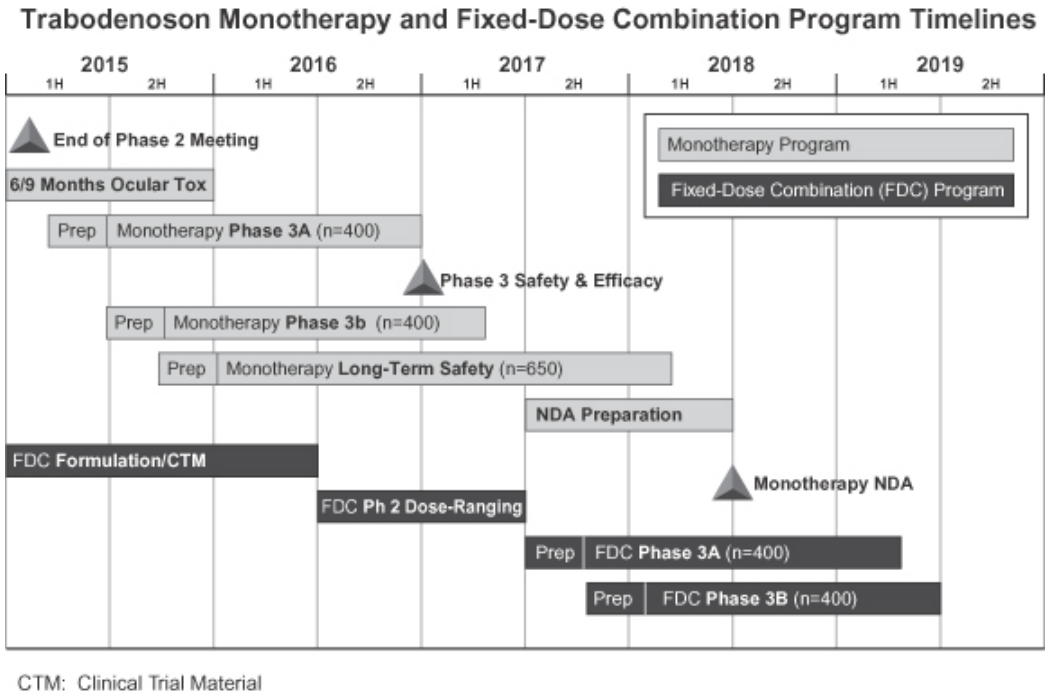
Efficacy (IOP-lowering), tolerability, safety and pharmacokinetics assessments were performed following study drug administration, and dose escalation from one cohort to the next cohort proceeded only after masked review of the safety data from the preceding cohort.

Conclusions

In conclusion, *trabodenoson* monotherapy ophthalmic solution up to and including 700 mcg were well-tolerated. This preliminary formulation of *trabodenoson* demonstrated activity at lowering IOP following single doses of 350 mcg and 700 mcg in patients with POAG or OHT.

Development Plans

Upon completion of our Phase 2 trials and meeting with the FDA, we plan to continue developing *trabodenoson* as a monotherapy and an FDC with *latanoprost*, along with the neuroprotective potential of both to slow the loss of vision significantly more than attributable to IOP-lowering alone either in glaucoma patients or other rarer forms of optic nerve neuropathy. The figure below shows our plans for upcoming clinical trials.



CTM: Clinical Trial Material

Trabodenoson

We are planning an End-of-Phase 2 meeting with the FDA in the first half of 2015 to discuss our Phase 3 program for *trabodenoson* monotherapy and to confirm the design and endpoints for the Phase 3 pivotal trials. This program is scheduled to begin in mid-2015, when the manufacturing (in accordance with the current Good Manufacturing Practices, or cGMP), packaging and labeling of the study drug are complete. The preliminary design for the program, which is to be confirmed by the FDA, is expected to include doses and dose frequencies based on the Phase 2 clinical data. The two Phase 3 pivotal efficacy trials are expected to include between 800 and 1,500 patients, depending on the design and number of dosing arms in the study, and are expected to include patients with glaucoma and baseline IOPs in the mid-20s mmHg. Following a run-in period, the trials are expected to run for 12 weeks of active treatment with the primary endpoint of IOP-lowering over the day. *Timolol* will be used as the active comparator due to its long history of use as a glaucoma drug and the large amount of clinical data available on the drug, making it the comparator of choice in most recent FDA filings.

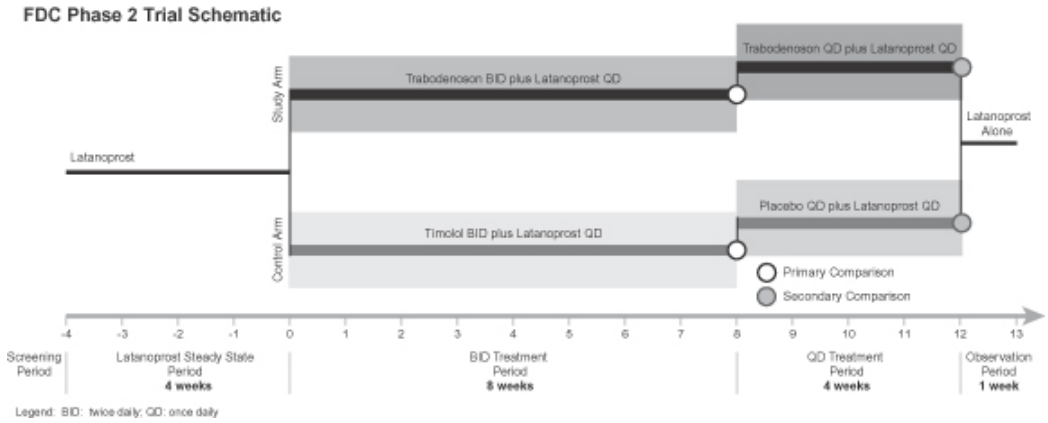
The FDA expects that a total of at least 1,500 patients are exposed to at least a single dose of *trabodenoson*, and the complete submission package must also contain safety data from at least 300 patients treated with *trabodenoson* for at least six months, and at least 100 patients treated for at least a year. These longer-term treatments will be accomplished in a long-term safety trial conducted at the highest anticipated *trabodenoson* dose, and with a *timolol* control, and are expected to begin in early

2016 when the long-term ocular toxicity studies of six and nine month durations are available to support the longer dosing time. This long-term safety trial represents the first opportunity for us to study the rate of vision loss over a longer time. If the enrollment projections are met, the first data from our Phase 3 program is anticipated in late 2016 or early 2017. We are planning to complete the long-term safety study in early 2018. If the primary objectives of our Phase 3 program are met, we plan to submit an NDA to the FDA for marketing approval of *trabodenoson* for the treatment of glaucoma in the United States.

Fixed-Dose Combination of Trabodenoson and Latanoprost

We are also developing an FDC of *trabodenoson* and *latanoprost*. Upon successful completion of our formulation efforts and stability studies, we will commence manufacturing of clinical supplies to support further clinical trials. We have not filed a separate investigational new drug application, or IND, for the FDC, as we expect to be able to rely on the existing *trabodenoson* IND. Similarly, we have not conducted a Phase 1 trial for the FDC as we were able to rely on the safety and tolerability data generated in our completed trials for *trabodeonson* as a monotherapy.

In August 2013, we commenced a Phase 2 trial in patients with OHT or POAG in which *trabodenoson* eye drops are co-administered with *latanoprost* eye drops. The trial is randomized, placebo- and active-controlled, and will enroll approximately 100 patients. The objective of the study is to evaluate the efficacy and safety of these two drugs when given concurrently to the same eye. Following four weeks of *latanoprost* eye drops, patients with an IOP greater than 24 mmHg are randomized to either *trabodenoson* BID plus *latanoprost* QD (study-arm) or *timolol* BID plus *latanoprost* QD (control-arm) for a total of eight weeks. At the end of the eight weeks, patients in the study-arm are switched to *trabodenoson* QD plus *latanoprost* QD, and patients in the control-arm are switched to placebo QD plus *latanoprost* QD and treatment is continued for an additional four weeks. This trial is designed to measure the additional IOP-lowering effect of *trabodenoson* when added to a PGA (*latanoprost*) and to compare this effect to the standard of care often given to the more severe glaucoma patient (*timolol* plus *latanoprost*). This trial will also measure the efficacy of QD *trabodenoson* plus *latanoprost* compared to *latanoprost* alone. Results of this trial are expected in late 2014. The schematic for this trial is below.



We expect results of the ongoing Phase 2 trial to provide efficacy and safety data for the combination of *latanoprost* and *trabodenoson*, at two dose levels, and when given QD and BID. These data will inform the format of the next study which will be structured to evaluate the safety and efficacy of various dose combinations and dosing patterns of an FDC of *latanoprost* and *trabodenoson*, which we still need to formulate. Once the results of this study are available, we believe that the FDA will

allow us to continue the Phase 2 development using several FDC formulations with various doses. However, the commencement of our Phase 2 program for the FDC product candidate will depend on successful development and cGMP manufacturing of stable FDC dosage forms. We expect to initiate our Phase 2 program in 2016 and plan to start our Phase 3 FDC program in late 2017. We expect our FDC product candidate to benefit many patients with higher IOPs and more severe disease that typically require more aggressive medical treatment. For this reason, the patient population for the FDC program is expected to carry a higher disease burden. As with the monotherapy product development, the FDA requirements for long-term dosing data (at least 300 patients treated with the FDC for at least six months, and at least 100 patients treated for at least a year) will require the program to include a long-term safety study.

Neuroprotection

We plan to study the neuroprotective potential of *trabodenoson* monotherapy and our FDC product candidate to slow the loss of vision significantly more than attributable to IOP-lowering alone either in glaucoma patients or other rarer forms of optic nerve neuropathy. While supported by the basic biology of adenosine, we have not yet conducted a formal program of studies to prove neuroprotection and have not filed an IND related to this program. This evaluation may include longer longitudinal studies in glaucoma patients, as potentially smaller patient groups with rapidly-progressing optic nerve damage. Although treatment times will be measured in years rather than months, this effort can run in parallel to the normal development trials, or may be included in the objectives of the planned long-term safety trials. The regulatory path for such an indication is thus far uncharted, so significant regulatory as well as clinical risk is anticipated for such a program and close interaction with regulatory agencies will be required. Due to the speculative nature of the development, it is difficult at this time to predict if or when an NDA submission in support of neuroprotection indication may be submitted.

Competition

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our experience and scientific knowledge provide us with competitive advantages, we face competition from established branded and generic pharmaceutical companies, such as Novartis International AG and its subsidiary Alcon Labs, Allergan Inc., Bausch + Lomb, Inc. (now a unit of Valeant Pharmaceuticals International, Inc.), Merck & Co., Inc., Santen Inc., Aerie Pharmaceuticals, Inc. and smaller biotechnology and pharmaceutical companies, as well as from academic institutions, government agencies and private and public research institutions, which may in the future develop products to treat glaucoma. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. We believe that the key competitive factors affecting the success of our product candidates, if approved, are likely to be efficacy, safety, convenience, price, tolerability and the availability of coverage and adequate reimbursement from governmental authorities and other third-party payors.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Glaukos Corporation recently commercialized a trabecular micro-bypass stent that is implanted in the eye during cataract surgery and allows fluid to flow from the anterior of the eye into the collecting channels, bypassing the TM. In addition, early-stage companies that are also developing glaucoma treatments, such as Aerie Pharmaceuticals, Inc., which is developing a Rho kinase/norepinephrine transport inhibitor, may prove to be significant competitors. We expect that our competitors will continue to develop new glaucoma treatments, which may include eye drops, oral treatments, surgical procedures, implantable devices or laser treatments.

Other early-stage companies may also compete through collaborative arrangements with large and established companies. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors.

These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer adverse effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours. In addition, our ability to compete may be affected because in many cases physicians, insurers or other third-party payors may encourage the use of generic products. The market for glaucoma prescriptions is highly competitive and is currently dominated by generic drugs, such as *latanoprost* and *timolol*, and additional products are expected to become available on a generic basis over the coming years. If any of our product candidates are approved, we expect that they will be priced at a premium over competitive generic products and consistent with other branded glaucoma drugs.

Manufacturing

Trabodenoson is a small molecule that is capable of being manufactured in reliable and reproducible synthetic processes from readily available starting materials. We believe the chemistry used to manufacture *trabodenoson* is amenable to a scale up and does not require unusual equipment in the manufacturing process. We do not currently operate manufacturing facilities for clinical or commercial production of our product candidates. We currently rely on third-party manufacturers to produce the active pharmaceutical ingredient and final drug product for our clinical trials. We manage such production with all our vendors on a purchase order basis in accordance with applicable master service and supply agreements. We do not have long-term agreements with these manufacturers or any other third-party suppliers. *Latanoprost* and *timolol*, used in our clinical trials, are available in commercial quantities from multiple reputable third-party manufacturers. We intend to procure quantities on a purchase order basis for our clinical and commercial production. If any of our existing third-party suppliers should become unavailable to us for any reason, we believe that there are a number of potential replacements, although we might experience a delay in our ability to obtain alternative suppliers. We also do not have any current contractual relationships for the manufacture of commercial supplies of our product candidates if they are approved. With respect to commercial production of our product candidates in the future, we plan to outsource production of the active pharmaceutical ingredients and final drug product manufacturing if they are approved for marketing by the applicable regulatory authorities.

We expect to continue to develop drug candidates that can be produced in a cost effective manner at contract manufacturing facilities. However, should a supplier or manufacturer on which we have relied to produce a product candidate provide us with a faulty product or such product is later recalled, we would likely experience delays and additional costs, each of which could be significant.

Intellectual Property

Our success depends in part on our ability to obtain and maintain proprietary protection for our products and product candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights.

We own a patent portfolio covering the *trabodenoson* compound that includes issued patents in the United States, Europe, Japan, and several other countries. These composition of matter patents are scheduled to expire by early 2026 in the United States and by mid-2025 abroad. We also own an issued U.S. patent and have pending patent applications in Europe and Japan relating to the use of *trabodenoson* for reducing IOP. The issued U.S. patent and the pending foreign patent applications, if

issued, are scheduled to expire by 2030. A detailed freedom-to-operate analysis has been conducted and we are not aware of any third party rights or impediments to commercializing *trabodenoson* for use in ophthalmic indications in the United States or Europe.

Our patent portfolio includes issued U.S. patents relating to combinations of *trabodenoson* with carbonic anhydrase inhibitors and beta blockers.

We are also pursuing patent applications in the United States and abroad relating to:

- combinations of *trabodenoson* with PGAs, carbonic anhydrase inhibitors or beta blockers, in patent applications which, if issued, are scheduled to expire by 2031;
- polymorphs of *trabodenoson*, in patent applications which, if issued, are scheduled to expire by 2033;
- formulations of *trabodenoson*, in patent applications which, if issued, are scheduled to expire by 2034; and
- ocular neuroprotective uses of *trabodenoson*, in patent applications which, if issued, are scheduled to expire by 2034.

As we advance the development of our *trabodenoson* products and clinical development we continue to look at opportunities to file additional patent applications covering new and innovative developments to ensure we have a patent portfolio that is multifaceted. For such additional applications, we will continue to seek patent protection in the United States and other jurisdictions that are important in the ophthalmic markets.

In addition to our patents and patent applications, we keep certain of our proprietary information as trade secrets, which we seek to protect by confidentiality agreements with our employees and third parties, and by seeking to maintain the physical security of our premises and physical and electronic security of our information technology systems.

Government Regulation

FDA Regulation and Marketing Approval

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act, or FDCA, and related regulations. Drugs are also subject to other federal, state and local statutes and regulations. Failure to comply with the applicable United States regulatory requirements at any time during the product development process, approval process or after approval may subject an applicant to administrative or judicial sanctions and non-approval of product candidates. These sanctions could include the imposition by the FDA or an Institutional Review Board, or IRB, of a clinical hold on trials, the FDA's refusal to approve pending applications or related supplements, withdrawal of an approval, untitled or warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, restitution, disgorgement, civil penalties or criminal prosecution. Such actions by government agencies could also require us to expend a large amount of resources to respond to the actions. Any agency or judicial enforcement action could have a material adverse effect on us.

The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements upon the clinical development, manufacture and marketing of pharmaceutical products. These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, post-approval monitoring, advertising, promotion, sampling and import and export of our products. Our drugs must be approved by the FDA through the NDA process before they may be legally marketed in the United States. See "The NDA Approval Process" below.

The process required by the FDA before drugs may be marketed in the United States generally involves the following:

- completion of non-clinical laboratory tests, animal studies and formulation studies conducted according to Good Laboratory Practices, or GLP, or other applicable regulations;
- submission of an IND, which allows clinical trials to begin unless FDA objects within 30 days;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug for its intended use or uses conducted in accordance with FDA regulations and Good Clinical Practices, or GCP, which are international ethical and scientific quality standards meant to ensure that the rights, safety and well-being of trial participants are protected and that the roles of clinical trial sponsors, administrators, and monitors are well defined;
- preparation and submission to the FDA of an NDA;
- review of the product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion pre-approval inspection of manufacturing facilities and clinical trial sites at which the product, or components thereof, are produced to assess compliance with cGMP requirements and of selected clinical trial sites to assess compliance with GCP requirements; and
- FDA approval of an NDA which must occur before a drug can be marketed or sold.

Preclinical Studies

Preclinical studies include laboratory evaluation of the purity and stability of the manufactured drug substance or active pharmaceutical ingredient and the formulated drug or drug product, as well as in vitro and animal studies to assess the safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, are submitted to the FDA as part of an IND.

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

IND and Clinical Trials

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Prior to commencing the first clinical trial, an initial IND, which contains the results of preclinical testing along with other information, such as information about product chemistry, manufacturing and controls and a proposed protocol, must be submitted to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA unless the FDA within the 30-day time period raises concerns or questions about the conduct of the clinical trial and imposes a clinical hold. A clinical hold may also be imposed at any time while the IND is in effect. In such a case, the IND sponsor must resolve any outstanding concerns with the FDA before the clinical trial may begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence.

A sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA or IND so long as the clinical trial is conducted in compliance with GCP, and the FDA is able to validate the data from the study through an onsite inspection if the agency deems it necessary.

A separate submission to the existing IND must be made for each successive clinical trial to be conducted during product development. Further, an independent IRB for each site proposing to conduct the clinical trial must review and approve the study for any clinical trial before it commences at that site. Informed written consent must also be obtained from each trial subject. Regulatory authorities, including the FDA, an IRB, a data safety monitoring board or the sponsor, may suspend or terminate a clinical trial at any time on various grounds, including a finding that the participants are being exposed to an unacceptable health risk or that the clinical trial is not being conducted in accordance with FDA requirements.

For purposes of NDA approval, human clinical trials are typically conducted in sequential phases that may overlap:

- Phase 1– the drug is initially given to healthy human subjects or patients and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. These trials may also provide early evidence on effectiveness. During Phase 1 clinical trials, sufficient information about the investigational drug's pharmacokinetics and pharmacologic effects may be obtained to permit the design of well-controlled and scientifically valid Phase 2 clinical trials.
- Phase 2– trials are conducted in a limited number of patients in the target population to identify possible adverse effects and safety risks, to determine the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3– when Phase 2 evaluations demonstrate that a dosage range of the product appears effective and has an acceptable safety profile, and provide sufficient information for the design of Phase 3 trials, Phase 3 trials are undertaken to provide statistically significant evidence of clinical efficacy and to further test for safety in an expanded patient population at multiple clinical trial sites. They are performed after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to further evaluate dosage, effectiveness and safety, to establish the overall benefit-risk relationship of the investigational drug and to provide an adequate basis for product labeling and approval by the FDA. In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the drug.

All clinical trials must be conducted in accordance with FDA regulations, GCP requirements and their protocols in order for the data to be considered reliable for regulatory purposes. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all.

An investigational drug product that is a combination of two different drugs in a single dosage form must comply with an additional rule that requires that each component make a contribution to the claimed effects of the drug product and the dosage of each component (amount, frequency, duration) is such that the combination is safe and effective for a significant patient population requiring such concurrent therapy as defined in the labeling of the drug product. This typically requires larger studies that test the drug against each of its components. In addition, typically, if a drug product is intended to

treat a chronic disease, as is the case with our products, safety and efficacy data must be gathered over an extended period of time, which can range from six months to three years or more.

Government regulation may delay or prevent marketing of product candidates or new drugs for a considerable period of time and impose costly procedures upon our activities.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA-regulated products, including drugs, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

The NDA Approval Process

In order to obtain approval to market a drug in the United States, a marketing application must be submitted to the FDA that provides data establishing to the FDA's satisfaction the safety and effectiveness of the investigational drug for the proposed indication. Each NDA submission requires a substantial user fee payment unless a waiver or exemption applies. The application includes all relevant data available from pertinent non-clinical or preclinical studies and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators that meet GCP requirements.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 1 or 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the end of Phase 2 meetings to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 trials that they believe will support approval of the new drug.

The results of product development, non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. It may request additional information rather than accept a NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. The FDA has 60 days from its receipt of an NDA to conduct an initial review to determine whether the application will be accepted for filing based on the agency's threshold determination that the application is sufficiently complete to permit substantive review. If the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. The FDA has agreed to specific performance goals on the review of NDAs and seeks to review standard NDAs in 12 months from submission of the NDA. The review process may be extended by the FDA for three additional months to consider certain late-submitted information or information intended to clarify information already provided in the submission. After the FDA completes its initial review of an NDA, it

will communicate to the sponsor that the drug will either be approved, or it will issue a complete response letter to communicate that the NDA will not be approved in its current form and inform the sponsor of changes that must be made or additional clinical, non-clinical or manufacturing data that must be received before the application can be approved, with no implication regarding the ultimate approvability of the application or the timing of any such approval, if ever. If or when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. FDA has committed to reviewing such resubmissions in two to six months depending on the type of information included. The FDA may refer applications for novel drug products or drug products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and, if so, under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical sites to assure compliance with GCP. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it typically will outline the deficiencies and often will request additional testing or information. This may significantly delay further review of the application. If the FDA finds that a clinical site did not conduct the clinical trial in accordance with GCP, the FDA may determine the data generated by the clinical site should be excluded from the primary efficacy analyses provided in the NDA. Additionally, notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

The FDA may require, or companies may pursue, additional clinical trials after a product is approved. These so-called Phase 4 trials may be made a condition to be satisfied for continuing drug approval. The results of Phase 4 trials can confirm the effectiveness of a product candidate and can provide important safety information. In addition, the FDA has authority to require sponsors to conduct post-marketing trials to specifically address safety issues identified by the agency. See "Post-Marketing Requirements" below.

The FDA also has authority to require a Risk Evaluation and Mitigation Strategy, or a REMS, from manufacturers to ensure that the benefits of a drug outweigh its risks. A sponsor may also voluntarily propose a REMS as part of the NDA submission. The need for a REMS is determined as part of the review of the NDA. Based on statutory standards, elements of a REMS may include "Dear Doctor letters," a medication guide, more elaborate targeted educational programs, and in some cases elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patient registries. These elements are negotiated as part of the NDA approval, and in some cases the approval date may be delayed. Once adopted, REMS are subject to periodic assessment and modification.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

Even if a product candidate receives regulatory approval, the approval may be limited to specific disease states, patient populations and dosages, or might contain significant limitations on use in the form of warnings, precautions or contraindications, or in the form of onerous risk management plans, restrictions on distribution, or post-marketing trial requirements. Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. Delay in obtaining, or failure to obtain, regulatory approval for our products, or obtaining approval but for significantly limited use, would harm our business. In addition, we cannot predict what adverse governmental regulations may arise from future United States or foreign governmental action.

The Hatch-Waxman Amendments

Under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, a portion of a product's U.S. patent term that was lost during clinical development and regulatory review by the FDA may be restored by returning up to five years of patent life for a patent that covers a new product or its use. This period is generally one-half the time between the effective date of an IND (falling after issuance of the patent) and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application, provided the sponsor acted with diligence. Patent term restorations, however, cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended and the extension must be applied for prior to expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

Market Exclusivity

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain competing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an Abbreviated New Drug Application, or ANDA, or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the non-clinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data.

Post-Marketing Requirements

Following approval of a new product, a pharmaceutical company and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting to the applicable regulatory authorities of adverse experiences with the product, providing the regulatory authorities with updated safety and efficacy information, product sampling and distribution requirements, and complying with promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, restrictions on promoting drugs for uses or in patient populations that are not described in the drug's approved labeling, or off-label use, limitations on industry-sponsored scientific and educational activities and requirements for promotional activities involving the internet. Although physicians may, in their independent professional medical judgment, prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses. Modifications or enhancements to the product or its labeling or changes of the site of manufacture are often subject to the approval of the FDA and other regulators, who may or may not grant approval or may include a lengthy review process.

Prescription drug advertising is subject to federal, state and foreign regulations. In the United States, the FDA regulates prescription drug promotion, including direct-to-consumer advertising. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Any distribution of prescription drug products and pharmaceutical samples must comply with the U.S. Prescription Drug Marketing Act, or the PDMA, a part of the FDCA.

In the United States, once a product is approved, its manufacturing is subject to comprehensive and continuing regulation by the FDA. The FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMP. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. These regulations also impose certain organizational, procedural and documentation requirements with respect to manufacturing and quality assurance activities. NDA holders using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These firms and, where applicable, their suppliers are subject to inspections by the FDA at any time, and the discovery of violative conditions, including failure to conform to cGMP, could result in enforcement actions that interrupt the operation of any such product or may result in restrictions on a product, manufacturer, or holder of an approved NDA, including, among other things, recall or withdrawal of the product from the market.

In addition, the manufacturer and/or sponsor under an approved NDA are subject to annual product and establishment fees. These fees are typically increased annually.

The FDA also may require post-marketing testing, also known as Phase 4 testing, REMS to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product. Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, untitled or warning letters from the FDA, mandated corrective advertising or communications with doctors, withdrawal of approval, and civil or

criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

Coverage and Reimbursement

Sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of reimbursement from third-party payors, including government healthcare program administrative authorities, managed care organizations, private health insurers, and other entities. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payors to reimburse all of part of the costs associated with their prescription drugs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Therefore, our products, once approved, may not obtain market acceptance unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products.

The process for determining whether a third-party payor will provide coverage for a drug product typically is separate from the process for setting the price of a drug product or for establishing the reimbursement rate that the payor will pay for the drug product once coverage is approved. Third-party payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the FDA-approved drugs for a particular indication. A decision by a third-party payor not to cover our product candidates could reduce physician utilization of our products once approved. Moreover, a third-party payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Additionally, coverage and reimbursement for drug products can differ significantly from payor to payor. One third-party payor's decision to cover a particular drug product or service does not ensure that other payors will also provide coverage for the medical product or service, or will provide coverage at an adequate reimbursement rate. As a result, the coverage determination process will require us to provide scientific and clinical support for the use of our products to each payor separately and will be a time-consuming process.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. Third-party payors are increasingly challenging the prices charged for drug products and medical services, examining the medical necessity and reviewing the cost effectiveness of drug products and medical services, in addition to questioning safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after FDA approval or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit.

In particular, our success may depend on our ability to obtain coverage and adequate reimbursement through Medicare Part D plans for our products that obtain regulatory approval. The Medicare Part D program provides a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities which will provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Part A and B, Part D coverage is not standardized. In general, Part D prescription drug plan sponsors have flexibility regarding coverage of Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level.

However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class, with certain exceptions. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for products for which we receive regulatory approval. However, any negotiated prices for our future products covered by a Part D prescription drug plan will likely be discounted, thereby lowering the net price realized on our sales to pharmacies. Moreover, while the Part D program applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from Medicare Part D may result in a similar reduction in payments from non-government payors.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research will be developed by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures will be made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of our product candidates, if any such product or the condition that it is intended to treat is the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of our product candidates, once approved. If third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally tend to be significantly lower.

Anti-Kickback and False Claims Laws and Other Regulatory Matters

In the United States, among other things, the research, manufacturing, distribution, sale and promotion of drug products and medical devices are potentially subject to regulation and enforcement by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare & Medicaid Services, other divisions of the United States Department of Health and Human Services (e.g., the Office of Inspector General), the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency, state Attorneys General and other state and local government agencies. Our current and future business activities, including for example, sales, marketing and scientific/educational grant programs must comply with healthcare regulatory laws, including the Federal Anti-Kickback Statute, the Federal False Claims Act, as amended, the privacy regulations promulgated under the Health Insurance Portability and Accountability Act, or HIPAA, as amended, physician payment transparency laws, and similar state laws. Pricing and rebate programs must comply with the Medicaid Drug Rebate Program requirements of the Omnibus Budget

Reconciliation Act of 1990, as amended, and the Veterans Health Care Act of 1992, as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. The handling of any controlled substances must comply with the U.S. Controlled Substances Act and Controlled Substances Import and Export Act. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. All of these activities are also potentially subject to federal and state consumer protection and unfair competition laws.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The Federal Anti-Kickback Statute makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer, or pay any remuneration that is intended to induce the referral of business, including the purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of, any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as Medicare or Medicaid. The term “remuneration” has been broadly interpreted to include anything of value. The Federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Federal Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Additionally, the intent standard under the Federal Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act, as amended by the Health Care Education and Reconciliation Act, or collectively the ACA, to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA codified case law that a claim including items or services resulting from a violation of the Federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the Federal False Claims Act. Violations of this law are punishable by up to five years in prison, criminal fines, administrative civil money penalties, and exclusion from participation in federal healthcare programs. In addition, many states have adopted laws similar to the Federal Anti-Kickback Statute. Some of these state prohibitions apply to the referral of patients for healthcare services reimbursed by any insurer, not just federal healthcare programs such as Medicare and Medicaid. Due to the breadth of these federal and state anti-kickback laws, and the potential for additional legal or regulatory change in this area, it is possible that our future business activities, including our sales and marketing practices and/or our future relationships with ophthalmologists and optometrists might be challenged under anti-kickback laws, which could harm us.

The Federal False Claims Act prohibits anyone from, among other things, knowingly presenting, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services, including drugs, that are false or fraudulent. This statute has been interpreted to prohibit presenting claims for items or services not provided as claimed, or claims for medically unnecessary items or services. Although we would not submit claims directly to payors, manufacturers can be held liable under these laws if they are deemed to “cause” the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. In addition, our future activities relating to the reporting of wholesaler or estimated

retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law. For example, pharmaceutical companies have been found liable under the Federal False Claims Act in connection with their off-label promotion of drugs. Penalties for a False Claims Act violation include three times the actual damages sustained by the government, plus mandatory civil penalties of between $5,500 and $11,000 for each separate false claim, the potential for exclusion from participation in federal healthcare programs, and, although the Federal False Claims Act is a civil statute, conduct that results in a False Claims Act violation may also implicate various federal criminal statutes. If the government were to allege that we were, or convict us of, violating these false claims laws, we could be subject to a substantial fine and may suffer a decline in our stock price. In addition, private individuals have the ability to bring actions under the Federal False Claims Act and certain states have enacted laws modeled after the Federal False Claims Act.

Similarly, the civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

Additionally, HIPAA created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.

There are also an increasing number of state laws that require manufacturers to make reports to states on pricing and marketing information. Many of these laws contain ambiguities as to what is required to comply with the laws. In addition, as discussed below, a similar federal requirement requires certain manufacturers to track and report to the federal government certain payments provided to physicians and teaching hospitals made in the previous calendar year. These laws may affect our sales, marketing and other promotional activities by imposing administrative and compliance burdens on us. In addition, given the lack of clarity with respect to these laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent state and federal authorities.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, including the final omnibus rule published on January 25, 2013, imposes specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to business associates, defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

The failure to comply with regulatory requirements subjects us to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result

in significant criminal, civil and/or administrative penalties, damages, fines, disgorgement, exclusion from participation in federal healthcare programs, such as Medicare and Medicaid, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, refusal to allow us to enter into supply contracts, including government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

We plan to develop a comprehensive compliance program that establishes internal controls to facilitate adherence to the law and program requirements to which we will or may become subject because we intend to commercialize products that could be reimbursed under a federal healthcare program and other governmental healthcare programs.

Changes in law or the interpretation of existing law could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

Affordable Health Care Act and Other Reform Initiatives

In the United States and some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system directed at broadening the availability of healthcare and containing or lowering the cost of healthcare.

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

- The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services in exchange for state Medicaid coverage of most of the manufacturer's drugs. ACA made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs and biologic agents to 23.1% of average manufacturer price, or AMP, and adding a new rebate calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP.
- The ACA expanded the types of entities eligible to receive discounted 340B pricing, although, with the exception of children's hospitals, these newly eligible entities will not be eligible to receive discounted 340B pricing on orphan drugs used in orphan indications. In addition, because 340B pricing is determined based on AMP and Medicaid drug rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discounts to increase. The ACA imposed a requirement on manufacturers of branded drugs and biologic agents to provide a 50% discount off the negotiated price of branded drugs dispensed to Medicare Part D beneficiaries in the coverage gap (i.e., "donut hole").
- The ACA imposed an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications.

- The ACA included the Federal Physician Payments Sunshine Act, which required pharmaceutical manufacturers to track certain financial arrangements with physicians and teaching hospitals, including any “transfer of value” provided, as well as any ownership or investment interests held by physicians and their immediate family members. Covered manufacturers were required to begin collecting data on August 1, 2013 and submit reports on aggregate payment data to the government for the first reporting period (August 1, 2013— December 31, 2013) by March 31, 2014, and were required to report detailed payment data for the first reporting period and submit legal attestation to the completeness and accuracy of such data by June 30, 2014. Thereafter, covered manufacturers must submit reports by the 90th day of each subsequent calendar year. The information reported is expected to be publicly available on a searchable website in September 2014.
- The ACA established a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research. The research conducted by the Patient-Centered Outcomes Research Institute may affect the market for certain pharmaceutical products.
- The ACA created the Independent Payment Advisory Board which has the authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. Under certain circumstances, these recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings.
- The ACA established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation through 2019.

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

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation’s automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2024 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability.

European Union Drug Development

In the European Union, our products will also be subject to extensive regulatory requirements. As in the United States, medicinal products can only be marketed if an MAA from the competent regulatory agencies has been obtained, and the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trial regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the member state regimes. Under the current regime, before a clinical trial can be initiated it must be approved by two distinct bodies in each of the EU countries where the trial is to be conducted: the

National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. In addition, all serious adverse reactions to the investigated drug that occur during the clinical trial must be reported to the NCA and ECs of the Member State where they occurred.

The EU clinical trials legislation is currently undergoing a revision process mainly aimed at making more uniform and streamlining the clinical trials authorization process, simplifying adverse event reporting procedures, improving the supervision of clinical trials and increasing the transparency of clinical trials.

European Union Drug Review Approval

In the European Economic Area, or EEA, which is comprised of the 28 Member States of the European Union plus Norway, Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining an MAA. There are two types of MAAs: the Community MAA, which is issued by the European Commission through the Centralized Procedure based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, a body of the EMA, and which is valid throughout the entire territory of the EEA; and the National MAA, which is issued by the competent authorities of the Member States of the EEA and only authorized marketing in that Member State's national territory and not the EEA as a whole.

The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU. The National MAA is for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MAA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MAA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MAA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. If the RMS proposes to authorize the product, and the other Member States do not raise objections, the product is granted a national MAA in all the Member States where the authorization was sought. Before granting the MAA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Other Regulations

We are also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control and disposal of hazardous or potentially hazardous substances. We may incur significant costs to comply with such laws and regulations now or in the future.

Employees

We had three full-time employees as of July 31, 2014. None of our employees are represented by any collective bargaining unit. We believe that we maintain good relations with our employees.

Property and Facilities

Our headquarters is currently located in Lexington, Massachusetts, and consists of approximately 2,300 square feet of leased office space under a lease that expires on March 31, 2015. We will require

additional space and facilities as our business expands. We believe that suitable additional or alternative space would be available if required in the future on commercially reasonable terms.

Legal Proceedings

From time to time, we may become involved in litigation relating to claims arising from the ordinary course of business. Our management believes that there are currently no claims or actions pending against us, the ultimate disposition of which could have a material adverse effect on our results of operations, financial condition or cash flows.

MANAGEMENT

Directors and Executive Officers

The following table sets forth information regarding our executive officers and directors, including their respective ages and positions as of the date hereof:

Name	Age	Position
Executive Officers:		
David P. Southwell	53	President, Chief Executive Officer and Director
Rudolf Baumgartner, M.D.	55	Executive Vice President and Chief Medical Officer
William K. McVicar, Ph.D.	56	Executive Vice President and Chief Scientific Officer
Dale Ritter	63	Vice President—Finance
Non-Management Directors:		
Ittai Harel	47	Director
Paul G Howes	60	Director
Devang V. Kantesaria, M.D.	41	Director
A.N. “Jerry” Karabelas, Ph.D.	61	Director
Isai Peimer	37	Director
Martin Vogelbaum	51	Director

(1) Member of the Compensation Committee.
(2) Member of the Audit Committee.
(3) Member of the Nominating and Corporate Governance Committee.

The following is a biographical summary of the experience of our executive officers and directors:

Executive Officers

David P. Southwell has served as our President and Chief Executive Officer since July 2014, and as one of our directors since August 2014. Mr. Southwell received a B.A. from Rice University and an M.B.A. from Dartmouth College. From March 2010 to October 2012, Mr. Southwell served as Executive Vice President, Chief Financial Officer of Human Genome Sciences, Inc., or Human Genome Sciences, which is owned by GlaxoSmithKline plc. Prior to his time at Human Genome Sciences, Mr. Southwell served as Executive Vice President and Chief Financial Officer of Sepracor Inc. from July 1994 to July 2008. Mr. Southwell has also served on the board of directors of PTC Therapeutics Inc. since December 2005 and THL Credit, Inc. since June 2007. We believe that Mr. Southwell’s qualifications to sit on our board of directors include his broad experience serving on the boards of directors of public companies, his specific experience with public therapeutics companies and his executive leadership, managerial and business experience.

Rudolf Baumgartner, M.D. has served as our Executive Vice President and Chief Medical Officer since June 2007. Dr. Baumgartner received a B.S. and an M.D. from Pennsylvania State University and completed post-doctoral training at the University of Michigan and Johns Hopkins University.

William K. McVicar, Ph.D. joined us in September 2007 as Executive Vice President, Pharmaceutical Development and has served as our Executive Vice President and Chief Scientific Officer since January 2009. Dr. McVicar also served as our interim President from May 2013 until August 2014. Dr. McVicar received a B.S. from the State University of New York at Oneonta and a Ph.D. in Chemistry from the University of Vermont.

Dale Ritter joined us as a financial consultant in June 2014 and has served as our Vice President—Finance since August 2014. Mr. Ritter received a B.A. from Syracuse University and an M.B.A. from Babson College.

Non-Management Directors

Ittai Harel has served as one of our directors since March 2010. Since July 2006, Mr. Harel has served in various roles, most recently as general partner, at Pitango Venture Capital, a provider of seed, growth and late-stage capital for core life sciences and technology companies. In connection with these positions, Mr. Harel currently serves on numerous boards of directors, including Vertos Medical, Inc., Valeritas, Inc., Lifebond Ltd. and EarlySense Ltd., also serving as Chairman of the boards of directors of Lifebond Ltd. and EarlySense Ltd. From February 2002 to June 2006, Mr. Harel held pharmaceutical product development strategy and business development roles at Nektar Therapeutics, including serving as Director of Corporate Development. Mr. Harel received a B.S from Ben Gurion University and an M.B.A. from the Massachusetts Institute of Technology. We believe that Mr. Harel's qualifications to sit on our board of directors include his extensive board and management experience, including with development stage life sciences companies.

Paul G. Howes has served as one of our directors since September 2008. Mr. Howes also served as our President and Chief Executive Officer from September 2008 to May 2013. Prior to his time with us, Mr. Howes served as President of the Americas Region of Bausch + Lomb Incorporated, or Bausch + Lomb, which is owned by Valeant Pharmaceuticals International, Inc., from July 2003 to February 2007. Since May 2013, Mr. Howes has served as a member of the board of directors of various companies including: since May 2013, Kish Bancorp and Kish Bank, a financial conglomerate parent company and its community bank subsidiary; since November 2008, Prevent Blindness America, a vision-related charity for which Mr. Howes has served as Chairman since November 2013; since August 2014, ThromboGenics NV and ThromboGenics Inc., a global integrated biopharmaceutical company and its U.S.-based operating subsidiary. Mr. Howes received an A.B. from Harvard University and an M.B.A. from York University. We believe that Mr. Howes' qualifications to sit on our board of directors include the intimate knowledge of our operations he developed as our President and Chief Executive Officer, his experience working with a public biopharmaceutical company and his executive leadership, managerial and business experience.

Devang V. Kantesaria, M.D. has served as one of our directors since September 2011. Since June 2006, Dr. Kantesaria has been a managing member at Devon Park Associates, LLC, a provider of capital for therapeutics companies which Dr. Kantesaria co-founded. From February 2000 to February 2006, Dr. Kantesaria held venture capital investment and portfolio company development roles at TL Ventures, including as Principal. Dr. Kantesaria received a B.S. from the Massachusetts Institute of Technology and an M.D. from Harvard Medical School. We believe that Dr. Kantesaria's qualifications to sit on our board of directors include his extensive experience in investing in and advising pharmaceutical companies.

A.N. "Jerry" Karabelas, Ph.D. has served as one of our directors since July 2012 and previously served as one of our directors from February 2004 to January 2012, during which time he was the Chairman of our board. Since December 2001, Mr. Karabelas has been a managing member at Care Capital II, LLC and Care Capital III, LLC, or Care Capital, a provider of capital for entrepreneurial private and public companies developing pharmaceuticals. Prior to his work at Care Capital, from July 2000 to September 2001, Mr. Karabelas was Chairman at Novartis BioVentures, which is owned by Novartis AG, or Novartis, a provider of capital for life sciences companies across the biotech, medical devices and diagnostics industries, prior to which Mr. Karabelas was the Chief Executive Officer of Novartis Pharma AG, which is owned by Novartis. In connection with his work at Care Capital, Mr. Karabelas has served on numerous boards of directors of pharmaceutical and therapeutics companies, including Renovo, plc, Vanda Pharmaceuticals, Inc. and NitroMed, Inc. Since June 2013, Mr. Karabelas served as Chairman of Polyphor AG. Mr. Karabelas also served as a member of the boards of directors of SkyePharma, plc from May 2001 to May 2009 and Human Genome Sciences. Mr. Karabelas received a B.S. from the University of New Hampshire and a Ph.D. from the

Massachusetts College of Pharmacy. We believe that Mr. Karabelas' qualifications to sit on our board of directors include his extensive experience in working with publicly held pharmaceuticals companies, advising developing life sciences, therapeutics and pharmaceuticals companies and his executive leadership, managerial and business experience.

Isai Peimer has served as one of our directors since May 2013. He is a principal at MedImmune Ventures Inc., an investment company, a position he has held since August 2010. From September 2009 to August 2010, Mr. Peimer was an associate analyst at AllianceBernstein LP, a global asset management firm. From April 2008 to January 2009, he was a senior associate at Visium Asset Management, LP, a healthcare-focused investment fund. From June 2005 to April 2008, Mr. Peimer worked as an investment banker at J.P. Morgan & Co. and was a management consultant for the pharmaceutical and biotech sectors. In connection with his work at MedImmune Ventures, Inc., Mr. Peimer has served on numerous boards of directors of pharmaceutical and therapeutics companies, including Ambit Biosciences Corp., where he is a member of the Audit and Nominating and Corporate Governance Committees, Adheron Therapeutics Inc., where he is a member of the Compensation and Nominating and Corporate Governance Committees, and Corridor Pharmaceuticals, Inc., where he is a member of the Audit Committee. Mr. Peimer received a B.A. from Emory University and an M.B.A. from Dartmouth College. We believe that Mr. Peimer's qualifications to sit on our board of directors include his experience on numerous committees of boards of directors of pharmaceutical companies and his work in advising developing life sciences companies.

Martin Vogelbaum has served as one of our directors since April 2010. Since May 2005, Mr. Vogelbaum has been a Partner at Rho Ventures, or Rho, a venture capital investment firm focused on companies in the healthcare, information technology, new media and multiple other sectors. Mr. Vogelbaum has served on numerous boards of directors private and public of biopharmaceutical companies, including Cara Therapeutics, Inc., where he has been a director since July 2010, and NephroGenex, Inc. Mr. Vogelbaum has more than twenty years of experience investing in life sciences companies at various stages of development and has co-founded more than a half dozen companies. Mr. Vogelbaum received an A.B. from Columbia University. We believe that Mr. Vogelbaum's qualifications to sit on our board of directors include his experience in investing in and service on boards of directors of public and private biopharmaceuticals and therapeutics companies.

Composition of Our Board of Directors

Our board of directors currently consists of seven members, all of whom were elected pursuant to the board composition provisions of our Stockholders Agreement, which is described under "Certain Relationships and Related Party Transactions—Agreements with our Stockholders" in this prospectus. These board composition provisions will terminate immediately prior to the closing of this offering. Upon the termination of these provisions, there will be no further contractual obligations regarding the election of our directors. Our nominating and governance committee and board of directors may therefore consider a broad range of factors relating to the qualifications and background of nominees, which may include diversity and is not limited to race, gender or national origin. We have no formal policy regarding board diversity. Our nominating and governance committee's and board of directors' priority in selecting board members is identification of persons who will further the interests of our stockholders through his or her established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, knowledge of our business, understanding of the competitive landscape and professional and personal experiences and expertise relevant to our growth strategy. Our directors hold office until their successors have been elected and qualified or until the earlier of their resignation or removal.

Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering also provide that our directors may be removed only for

cause by the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

Director independence. Our board of directors has determined that all members of the board of directors, except Messrs. Howes and Southwell, are independent, as determined in accordance with the rules of The NASDAQ Global Market, or NASDAQ. In making such independence determination, the board of directors considered the relationships that each such non-employee director has with us and all other facts and circumstances that the board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director. In considering the independence of the directors listed above, our board of directors considered the association of our directors with the holders of more than 5% of our common stock. Upon the closing of this offering, we expect that the composition and functioning of our board of directors and each of our committees will comply with all applicable requirements of NASDAQ and the rules and regulations of the SEC. There are no family relationships among any of our directors or executive officers.

Staggered board. In accordance with the terms of our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering, our board of directors will be divided into three classes, class I, class II and class III, with each class serving staggered three-year terms. Upon the expiration of the term of a class of directors, directors in that class will be eligible to be elected for a new three-year term at the annual meeting of stockholders in the year in which their term expires.

- Our Class I directors will be and ;
- Our Class II directors will be and ; and
- Our Class III directors will be and .

Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering provide that the authorized number of directors may be changed only by resolution of the board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class shall consist of one third of the board of directors.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent stockholder efforts to effect a change of our management or a change in control.

Board Leadership Structure and Board's Role in Risk Oversight

The positions of our Chairman of the board and Chief Executive Officer are presently separated. Separating these positions allows our Chief Executive Officer to focus on our day-to-day business, while allowing the Chairman of the board to lead the board of directors in its fundamental role of providing advice to and independent oversight of management. Our board of directors recognizes the time, effort and energy that the Chief Executive Officer must devote to his position in the current business environment, as well as the commitment required to serve as our Chairman, particularly as the board of directors' oversight responsibilities continue to grow. Our board of directors also believes that this structure ensures a greater role for the independent directors in the oversight of our company and active participation of the independent directors in setting agendas and establishing priorities and procedures for the work of our board of directors. Our board of directors believes its administration of its risk oversight function has not affected its leadership structure. Although our amended and restated bylaws that will be in effect upon the closing of this offering will not require our Chairman and Chief

Executive Officer positions to be separate, our board of directors believes that having separate positions is the appropriate leadership structure for us at this time and demonstrates our commitment to good corporate governance.

Our board of directors oversees the management of risks inherent in the operation of our business and the implementation of our business strategies. Our board of directors performs this oversight role by using several different levels of review. In connection with its reviews of our operations and corporate functions, our board of directors addresses the primary risks associated with those operations and corporate functions. In addition, our board of directors reviews the risks associated with our business strategies periodically throughout the year as part of its consideration of undertaking any such business strategies.

Each of our board committees also oversees the management of our risk that falls within the committee's areas of responsibility. In performing this function, each committee has full access to management, as well as the ability to engage advisors. Our principal financial officer reports to the audit committee and is responsible for identifying, evaluating and implementing risk management controls and methodologies to address any identified risks. In connection with its risk management role, our audit committee meets privately with representatives from our independent registered public accounting firm and our principal financial officer. The audit committee oversees the operation of our risk management program, including the identification of the primary risks associated with our business and periodic updates to such risks, and reports to our board of directors regarding these activities.

Board Committees

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee, each of which operates pursuant to a separate charter adopted by our board of directors. The composition and functioning of all of our committees will comply with all applicable requirements of the Sarbanes-Oxley Act, the Dodd-Frank Act, NASDAQ and SEC rules and regulations.

Audit Committee

currently serve on the audit committee, which is chaired by . Our board of directors has determined that each member of the audit committee is "independent" for audit committee purposes as that term is defined in the rules of the SEC and the applicable rules of NASDAQ. Our board of directors has designated as an "audit committee financial expert," as defined under the applicable rules of the SEC. The audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our independent registered public accounting firm;
- approving auditing and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the internal audit plan with the independent registered public accounting firm and members of management responsible for preparing our financial statements;
- reviewing and discussing with management and the independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;
- reviewing the adequacy of our internal control over financial reporting;
- establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;
- recommending, based upon the audit committee's review and discussions with management and the independent registered public accounting firm, whether our audited financial statements shall be included in our Annual Report on Form 10-K;

- monitoring the integrity of our financial statements and our compliance with legal and regulatory requirements as they relate to our financial statements and accounting matters;
- preparing the audit committee report required by SEC rules to be included in our annual proxy statement;
- reviewing all related party transactions for potential conflict of interest situations and approving all such transactions; and
- reviewing quarterly earnings releases.

Compensation Committee

currently serve on the compensation committee, which is chaired by . Our board of directors has determined that each member of the compensation committee is "independent" as that term is defined in the applicable rules of NASDAQ. The compensation committee's responsibilities include:

- annually reviewing and approving corporate goals and objectives relevant to the compensation of our Chief Executive Officer;
- evaluating the performance of our Chief Executive Officer in light of such corporate goals and objectives and determining the compensation of our Chief Executive Officer;
- reviewing and approving the compensation of our other executive officers;
- reviewing and establishing our overall management compensation, philosophy and policy;
- overseeing and administering our compensation and similar plans;
- evaluating and assessing potential current compensation advisors in accordance with the independence standards identified in the applicable rules of NASDAQ;
- retaining and approving the compensation of any compensation advisors;
- reviewing and approving our policies and procedures for the grant of equity-based awards;
- reviewing and making recommendations to the board of directors with respect to director compensation;
- preparing the compensation committee report required by SEC rules to be included in our annual proxy statement;
- reviewing and discussing with management the compensation discussion and analysis to be included in our annual proxy statement or Annual Report on Form 10-K; and
- reviewing and discussing with the board of directors corporate succession plans for the Chief Executive Officer and other key officers.

Nominating and Corporate Governance Committee

currently serve on the nominating and corporate governance committee, which is chaired by . Our board of directors has determined that each member of the nominating and corporate governance committee is "independent" as that term is defined in the applicable rules of NASDAQ. The nominating and corporate governance committee's responsibilities include:

- developing and recommending to the board of directors criteria for board and committee membership;
- establishing procedures for identifying and evaluating board of director candidates, including nominees recommended by stockholders;
- identifying individuals qualified to become members of the board of directors;
- recommending to the board of directors the persons to be nominated for election as directors and to each of the board's committees;
- developing and recommending to the board of directors a set of corporate governance guidelines; and
- overseeing the evaluation of the board of directors and management.

Our board of directors may establish other committees from time to time.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee has at any time during the prior three years been one of our officers or employees. None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our board of directors or compensation committee.

Corporate Governance

Prior to the closing of this offering, we will adopt a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions. Following the completion of this offering, a current copy of the code will be posted on the Corporate Governance section of our website, which is located at www.inotekcorp.com. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

EXECUTIVE COMPENSATION

Executive Compensation Overview

Historically, our executive compensation program has reflected our growth and development-oriented corporate culture. To date, the compensation of David P. Southwell, our President and Chief Executive Officer, and the other executive officers identified in the Summary Compensation Table below, has consisted of a combination of base salary, bonuses and long-term incentive compensation in the form of stock options. Our executive officers and all salaried employees are also eligible to receive health and welfare benefits.

As we transition from a private company to a publicly-traded company, we will evaluate our compensation values and philosophy and compensation plans and arrangements as circumstances require. At a minimum, we expect to review executive compensation annually with input from a compensation consultant if and when determined appropriate by the compensation committee. As part of this review process, we expect the board of directors and the compensation committee to apply our values and philosophy, while considering the compensation levels needed to ensure our executive compensation program remains competitive. We will also review whether we are meeting our retention objectives and the potential cost of replacing a key employee.

Compensation Tables

Summary Compensation Table—2013

The following table presents information regarding the total compensation awarded to, earned by, and paid to each of our named executive officers for services rendered in all capacities to us for the year ended December 31, 2013.

Name and principal position	Salary ($)	Bonus ($)	Option awards ($)	Non-equity incentive plan compensation ($)	Total ($)
David P. Southwell(1) *President and Chief Executive Officer*	–	–	–	–	–
Rudolf Baumgartner, M.D. *Executive Vice President and Chief Medical Officer*	322,438	25,000(3)	–	–	347,438
William K. McVicar, Ph.D. *Executive Vice President and Chief Scientific Officer*	290,698	25,000(3)	–	–	315,698
Dale Ritter(4) *Vice President—Finance*	–	–	–	–	–
Paul G. Howes(2) *Former President and Chief Executive Officer*	371,289	–	–	–	371,289

(1) Mr. Southwell was not an employee of ours during the year ended December 31, 2013. In connection with the commencement of his employment, Mr. Southwell entered into an employment agreement with us as described below, was granted options to purchase 280,368 shares of our common stock and will receive an annual base salary of $300,000. Subject to certain conditions, 25% of the options we granted to Mr. Southwell vest on the first anniversary of the date of this offering and the remaining 75% of the options we granted to Mr. Southwell vest in equal monthly installments beginning on the first anniversary of this offering with all options becoming vested on August 29, 2018.

(2) Mr. Howes resigned as our President and Chief Executive Officer in May 2013.
(3) Reflects the amount paid under retention bonus agreements we entered into with Dr. Baumgartner and Dr. McVicar. The material terms of these retention agreements are described below in the “Executive Compensation—Employment Agreements with Our Named Executive Officers” section.
(4) Mr. Ritter was not an employee of ours during the year ended December 31, 2013. In connection with the commencement of his employment, Mr. Ritter entered into an employment agreement with us as described below, was granted options to purchase 178,476 shares of our common stock and will receive an annual base salary of $255,000. Subject to certain conditions, 25% of the options we granted to Mr. Ritter vest on the first anniversary of the commencement of his employment and the remaining 75% of the options we granted to Mr. Ritter vest in equal monthly installments beginning on the first anniversary of the commencement of his employment with all options becoming vested on August 28, 2018.

Employment Agreements with Our Named Executive Officers

We have entered into employment agreements with certain of our named executive officers. These employment agreements will provide for “at will” employment and contain the additional terms summarized below:

David P. Southwell. On August 11, 2014, we entered into an employment agreement with Mr. Southwell, our President and Chief Executive Officer. Mr. Southwell currently receives a base salary of $300,000, which is subject to review and adjustment in accordance with our corporate policy. Mr. Southwell is eligible for an annual performance bonus with a target amount of 30% of his base salary, pro-rated for 2014 based on Mr. Southwell’s start date with us, payable at the discretion of our board of directors or compensation committee. Mr. Southwell is eligible to participate in our employee benefit plans in effect from time to time, subject to the terms of those plans.

Rudolf Baumgartner, M.D. On May 2, 2007, we entered into an employment agreement with Dr. Baumgartner, our Executive Vice President and Chief Medical Officer, which we amended on December 23, 2008 and October 9, 2009. Dr. Baumgartner currently receives a base salary of $322,438, which is subject to review and adjustment in accordance with our corporate policy. Dr. Baumgartner is eligible for an annual performance bonus with a target amount of 25% of his base salary. Dr. Baumgartner is eligible to participate in our employee benefit plans in effect from time to time, subject to the terms of those plans. We also entered into a retention bonus agreement with Dr. Baumgartner on June 24, 2013 pursuant to which Dr. Baumgartner received a one-time retention bonus payment of $12,500, a one-time milestone bonus payment of $12,500 and, subject to certain terms and conditions, is eligible to receive up to $25,000 in additional bonus payments upon the completion of our Phase 2 trial.

William K. McVicar, Ph.D. On August 23, 2007, we entered into an employment agreement with Dr. McVicar, our Executive Vice President and Chief Scientific Officer, which we amended on December 23, 2008 and October 9, 2009. Dr. McVicar currently receives a base salary of $290,698, which is subject to review and adjustment in accordance with our corporate policy. Dr. McVicar is eligible for an annual performance bonus with a target amount of 20% of his base salary, payable at the discretion of our board of directors. Dr. McVicar is eligible to participate in our employee benefit plans in effect from time to time, subject to the terms of those plans. We also entered into a retention bonus agreement with Dr. McVicar on June 24, 2013 pursuant to which Dr. McVicar received a one-time retention bonus payment of $12,500, a one-time milestone bonus payment of $12,500 and, subject to certain terms and conditions, is eligible to receive up to $25,000 in additional bonus payments upon the completion of our Phase 2 trial.

Dale Ritter. On August 28, 2014, we entered into an employment agreement with Mr. Ritter, our Vice President—Finance. Mr. Ritter currently receives an annual base salary of $255,000. Mr. Ritter is eligible for an annual performance bonus with a target amount of 30% of his annualized base salary, pro-rated for 2014 based on Mr. Ritter's start date with us, payable at the discretion of our president and chief executive officer and our board of directors. Mr. Ritter is eligible to participate in our employee benefit plans in effect from time to time, subject to the terms of those plans.

Involuntary Termination of Employment and Change of Control

Subject to the execution and effectiveness of a separation agreement, including, among other things, a general release of claims, Mr. Southwell will be eligible to receive the following payments and benefits in the event that his employment is terminated by us without cause or he terminates his employment with us for good reason:

- base salary continuation for twelve months;
- if Mr. Southwell is participating in our group health plan immediately prior to the date of termination and elects COBRA health continuation, we will pay him a monthly cash payment equal to the monthly employer contribution we would have made to provide him health insurance if he had remained employed by us until twelve months following the date of termination; and
- the portion of the stock options and other time-based equity awards held by Mr. Southwell as of the date of termination that would have vested in the twelve months following termination of his employment had he remained employed by us through such date shall immediately accelerate and become fully vested as of the date of termination.

Subject to the execution and effectiveness of a separation agreement, including, among other things, a general release of claims, each of Dr. Baumgartner and Dr. McVicar will be eligible to receive the following payments and benefits in the event that his employment is terminated by us without cause:

- base salary continuation for twelve months; and
- with respect to Dr. Baumgartner, a monthly cash payment equal to the monthly employer contribution we would have made to provide him health and dental insurance coverage if he had remained employed by us until twelve months following the date of termination.

Subject to the execution and effectiveness of a separation agreement, including, among other things, a general release of claims, Mr. Ritter will be eligible to receive base salary continuation for six months in the event that his employment is terminated by us without cause.

The receipt of the severance payments and benefits set forth above shall be conditioned upon the named executive officer not violating the terms of a restrictive covenant agreement.

Subject to the execution and effectiveness of a separation agreement, including, among other things, a general release of claims, each named executive officer will be eligible to receive the payments and benefits set forth below in the event that his employment is terminated by us without cause or the named executive officer terminates his employment with us for good reason, in either case within twelve months after a "change in control." With the exception of the payments and benefits for which Mr. Southwell is eligible, the payments and benefits described below are in addition to, not in lieu of, the payments set forth above. With respect to Mr. Southwell, the payments and benefits described below are in lieu of the payments set forth above.

- A one-time lump payment equal to eighteen months base salary within forty-five days of termination for Mr. Southwell.

- All unvested stock options and other stock-based awards held by the named executive officer as of the date of the termination of such named executive officer's employment shall immediately accelerate and become fully vested as of the date of termination.

The receipt of the severance payments and benefits set forth above shall be conditioned upon the named executive officer not violating the terms of a restrictive covenant agreement.

Definitions

For purposes of the employment agreement with Mr. Southwell, "cause" means:

- material misconduct, deliberate and material violation of our rules or policies or breach of a fiduciary duty owed to us;
- commission of an act of fraud, theft, misappropriation or embezzlement;
- violation of a federal or state securities law;
- conviction of, or pleading *nolo contendre* to, a felony or any other crime involving moral turpitude;
- failure to use reasonable best efforts to consummate a potential change of control of Inotek with one or more potential acquirers following the initiation of a change of control process supported by our board of directors; or
- material breach of any written agreement with us which breach is not cured within ten days of written notice given by us specifying in reasonable detail such breach.

For purposes of the employment agreements with Dr. Baumgartner, Dr. McVicar and Mr. Ritter, "cause" means:

- misconduct, deliberate disregard of our rules or policies or breach of a fiduciary duty to us;
- commission of an act of fraud, theft, misappropriation or embezzlement;
- violation of federal or state securities laws;
- conviction of, or pleading *nolo contendere* to, a felony or any other crime involving moral turpitude; or
- material breach of the employment agreement, any stock option agreement between such named executive officer and us, the confidentiality agreement between such named executive officer and us, or any other written agreement between such named executive officer and us.

For purposes of the employment agreement with Mr. Southwell, "good reason" means the compliance with certain processes and procedures following the occurrence of any of the following events:

- reduction of base salary without the prior consent of such named executive officer other than in connection with and substantially proportionate to our reductions of the compensation of our management employees;
- material diminution in his duties, responsibilities and authorities with us without his prior consent; or
- relocation of our offices more than fifty miles away from the current location without his prior consent.

Notwithstanding the foregoing, in no event shall a named executive officer be deemed to have resigned for good reason unless such named executive officer provides written notice of the reason for such resignation within ninety days of the initial occurrence of such reason and we fail, with such named executive officer's good faith cooperation, to cure the situation within thirty days following such notice, provided that the resignation must occur no more than thirty days following the end of our cure period.

For the purposes of the employment agreements with Dr. Baumgartner, Dr. McVicar and Mr. Ritter, “good reason” means:

- reduction of compensation due to such named executive officer on the date of his employment agreement that is not part of a reduction applicable to our other senior executives or our failure to pay such named executive officer’s compensation in the time and manner contemplated therein;
- our requirement that such named executive officer relocate to an office more than 50 miles from our current office; or
- material reduction in such named executive officer’s title, responsibilities, duties, reporting relationships or authorities as they exist on the date of each employment agreement.

Notwithstanding the foregoing, in no event shall Dr. Baumgartner, Dr. McVicar or Mr. Ritter be deemed to have resigned for good reason unless such named executive officer provides written notice of the reason for such resignation within ninety days of the initial occurrence of such reason and we fail to cure the situation within thirty days following such notice.

For purposes of the employment agreements with Mr. Southwell, “change in control” means:

- our consolidation or merger into or with any other entity of entities (except such transaction into one of our subsidiaries or in which we are the surviving corporation and the holders of our voting stock outstanding immediately prior to such transaction constitute not less than the holders of a majority of the voting stock outstanding immediately following such transaction);
- our sale, lease, transfer or exclusive license of all or substantially all of our intellectual property relating to *trabodenoson* (other than a sale, lease, transfer or exclusive license of a subsidiary of ours or to an entity in which the holders of our voting stock outstanding immediately prior to such transaction constitute not less than the holders of a majority of the voting stock outstanding immediately following such transaction);
- our sale, lease transfer or exclusive license of substantially all of our assets (other than a sale, lease, transfer or exclusive license of a subsidiary of ours or to an entity in which the holders of our voting stock outstanding immediately prior to such transaction constitute not less than the holders of a majority of the voting stock outstanding immediately following such transaction); or
- the sale, exchange or transfer by our stockholders, in a single transaction or a series of related transactions, of capital stock representing a majority of the voting power at elections of our directors (other than a transaction or series of transactions in which we are the surviving entity and the holders of our voting stock outstanding immediately prior to such transaction or series of transactions constitute not less than the holders of a majority of the voting stock outstanding immediately following such transaction or series of transactions).

Notwithstanding the foregoing, a change in control shall not be deemed to have occurred solely as the result of an acquisition of securities by us which, by reducing the number of shares of voting securities outstanding, increases the proportionate number of voting securities beneficially owned by any person to 50% or more of the combined voting power of all of the then outstanding voting securities; provided, however, that if any person referred to in this sentence shall thereafter become the beneficial owner of any additional shares of voting securities (other than pursuant to a stock split, stock dividend or similar transaction or as a result of an acquisition of securities directly from us) and immediately thereafter beneficially owns 50% or more of the combined voting power of all of the then outstanding voting securities, then a change in control shall be deemed to have occurred.

For the purposes of the employment agreements with Dr. Baumgartner, Dr. McVicar and Mr. Ritter, “change in control” means:

- a sale of the company by merger in which our stockholders in their capacity as such no longer own a majority of our or our successor’s outstanding equity securities;
- any sale of all or substantially all of our assets or capital stock (other than in a spin-off or similar transaction); or
- any other acquisition of our business, as determined by our board of directors.

Outstanding Equity Awards at Fiscal Year-End Table—2013

The following table summarizes, for each of our named executive officers, the number of shares of common stock underlying outstanding stock options and restricted common stock held as of December 31, 2013.

	Option Awards		
Name	Number of securities underlying unexercised options (#) exercisable (1)	Per share option exercise price ($)	Option expiration date
David P. Southwell	–	–	–
Rudolf Baumgartner, M.D.	8,810	$ 10.00	6/3/2017
	805	$ 10.00	3/20/2018
William K. McVicar, Ph.D.	5,150	$ 10.00	9/18/2017
	1,880	$ 10.00	12/31/2018
	470	$ 10.00	3/20/2018
Dale Ritter	–	–	–
Paul G. Howes	25,000	$ 10.00	8/31/2018

(1) All options held by our named executive officers are fully vested as of December 31, 2013.

Director Compensation

The following table presents the total compensation for each person who served as a member of our board of directors during 2013. Other than as set forth in the table and described more fully below, we did not pay any compensation, make any equity awards or non-equity awards to, or pay any other compensation to any of the non-employee members of our board of directors in 2013. David P. Southwell, who is also our President and Chief Executive Officer, receives no compensation for his service as a director, and, consequently, is not included in this table.

We intend to put in place a formal director compensation policy for all of our non-employee directors prior to the closing of this offering.

Director Compensation Table—2013

Director name(1)	Fees earned or paid in cash ($)	Option awards ($)	All other compensation ($)	Total ($)
William Bertrand(2)	–	–	–	–
Ittai Harel	–	–	–	–
Paul G. Howes	–	–		
Devang V. Kantesaria, M.D.			–	
A.N. “Jerry” Karabelas, Ph.D.	–	–	–	–
Michael Loberg, Ph.D.(3)	–	–	–	–
Isai Peimer	–	–	–	–
Martin Vogelbaum	–	–	–	–

(1) As of December 31, 2013, none of our directors as of such date held stock awards and only the following directors as of such date held any stock options: Mr. Howes held 25,000 stock options and Dr. Loberg held 3,109 stock options.
(2) Mr. Bertrand resigned from our board of directors in May 2013.
(3) Dr. Loberg resigned from our board of directors in July 2014.

Compensation Risk Assessment

We believe that although a portion of the compensation provided to our executive officers and other employees is performance-based, our executive compensation program does not encourage excessive or unnecessary risk taking. This is primarily due to the fact that our compensation programs are designed to encourage our executive officers and other employees to remain focused on both short-term and long-term strategic goals, in particular in connection with our pay-for-performance compensation philosophy. As a result, we do not believe that our compensation programs are reasonably likely to have a material adverse effect on us.

Equity Compensation Plans and Other Benefit Plans

The equity incentive plans described in this section are our 2004 Stock Option and Incentive Plan, or the 2004 Plan and our 2014 Stock Option and Incentive Plan, or 2014 Plan. Prior to this offering, we granted awards to eligible participants under the 2004 Plan until its expiration date in February 2014 and the 2014 Plan. We expect to continue to grant awards to eligible participants under the 2014 Plan following the closing of this offering. The following descriptions of certain transactions, payments and other matters contemplated by the 2004 Plan and the 2014 Plan are summaries only. They do not purport to be complete and are qualified, in all respects, by the actual provisions of the 2004 Plan and the 2014 Plan.

2004 Plan

The 2004 Plan was approved by our board of directors and our stockholders on February 10, 2004 and was amended in August 2005 and in September 2008. The 2004 Plan provides for the grant of incentive stock options, as defined under Section 422 of the Code, and for the grant of non-statutory stock options, restricted stock and other equity interests to our employees, officer, directors, consultants and advisors.

As of June 30, 2014, options to purchase a total of 48,137 shares of common stock, with a weighted average exercise price of $10.00 per share, remained outstanding under the 2004 Plan. The 2004 Plan has expired and we therefore no longer issue any additional awards under the 2004 Plan.

Although no future awards may be granted under the 2004 Plan, all grants previously granted under the 2004 Plan will continue to be outstanding and will be governed under the terms and conditions of the 2004 Plan. Our 2004 Plan is administered by our board of directors. Our board of directors has the authority to accelerate the exercisability or vesting of any award and to determine the specific terms and conditions of each award, subject to the provisions of the 2004 Plan. All stock option awards that were granted pursuant to the 2004 Plan are covered by an option agreement, and all restricted stock awards that were granted pursuant to the 2004 Plan are covered by a restricted stock purchase agreement.

The 2004 Plan provides that upon the occurrence of an “Acquisition,” as defined in the 2004 Plan, the board of directors of the surviving or acquiring entity shall, as to outstanding awards, make appropriate provision for the continuation of such awards or the assumption of such awards by the surviving or acquiring entity, or by substituting on an equitable basis for the shares subject to the awards either the consideration payable in the Acquisition, stock of the surviving corporation or securities or other consideration as our board of directors deems appropriate with a fair market value

not materially different from the stock subject to such awards immediately prior to the acquisition. Our board of directors may also provide that outstanding options must be exercised within a specified number of days, after which the options shall terminate or provide that one or more awards shall be terminated in exchange for a cash payment equal to the excess of the fair market value of the shares over the exercise price thereof.

Our board of directors may amend, alter, suspend or terminate the 2004 Plan at any time. Our board of directors may also amend, modify or terminate any outstanding award, provided that no amendment to an award may materially impair any of the rights of a participant under any awards previously granted without his or her written consent.

2014 Plan

On 2014, our board of directors adopted and our stockholders approved our 2014 Plan to replace the 2004 Plan. Our 2014 Plan provides us flexibility to use various equity-based incentive and other awards as compensation tools to motivate our workforce. These tools include stock options, stock appreciation rights, restricted stock, restricted stock units, unrestricted stock, performance share awards, cash-based awards and dividend equivalent rights. The 2014 Plan will become effective on the date immediately preceding the closing of this offering.

We have initially reserved shares of common stock for the issuance of awards under the 2014 Plan. The shares we issue pursuant to awards granted under the 2014 Plan will be authorized but unissued shares or shares that we reacquire. The shares of common stock underlying any awards that are forfeited, cancelled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, reacquired by us prior to vesting, satisfied without any issuance of common stock, expire or are otherwise terminated (other than by exercise) under the 2014 Plan and the 2004 Plan will be added back to the shares available for issuance under the 2014 Plan.

Under the 2014 Plan, stock options or stock appreciation rights with respect to no more than shares of common stock may be granted to any one individual in any one calendar year and the maximum number of shares that may be issued in the form of incentive stock options in any one calendar year period may not exceed shares.

The 2014 Plan will be administered by the compensation committee. The compensation committee has full power to select, from among the individuals eligible for awards, the individuals to whom awards will be granted, to make any combination of awards to participants, and to determine the specific terms and conditions of each award, subject to the provisions of the 2014 Plan. Full and part-time officers, employees, non-employee directors and other key persons (including consultants) as selected from time to time by our compensation committee will be eligible to participate in the 2014 Plan.

The 2014 Plan permits the granting of both options to purchase common stock intended to qualify as incentive stock options under Section 422 of the Code and options that do not so qualify. The exercise price of each stock option will be determined by the compensation committee but may not be less than 100% of the fair market value of our common stock on the date of grant or, in the case of an incentive stock option granted to a 10% owner, less than 110% of the fair market value of our common stock on the date of grant. The term of each stock option will be fixed by the compensation committee and may not exceed 10 years from the date of grant (or five years in the case of an incentive stock option granted to a 10% owner). The compensation committee will determine at what time or times each option may be exercised.

The compensation committee may award stock appreciation rights subject to such conditions and restrictions as it may determine. Stock appreciation rights entitle the recipient to shares of common

stock, or cash, equal to the value of the appreciation in our stock price over the exercise price. The exercise price of each stock appreciation right may not be less than 100% of fair market value of the common stock on the date of grant.

The compensation committee may award restricted shares of common stock or restricted stock units to participants subject to such conditions and restrictions as it may determine. These conditions and restrictions may include the achievement of certain performance goals and/or continued employment or service with us through a specified vesting period. The compensation committee may also grant cash-based awards to participants subject to such conditions and restrictions as it may determine. The compensation committee may also grant shares of common stock that are free from any restrictions under the 2014 Plan. Unrestricted stock may be granted to participants in recognition of past services or for other valid consideration and may be issued in lieu of cash compensation due to such participant.

The compensation committee may grant performance share awards to participants that entitle the recipient to receive awards of common stock upon the achievement of certain performance goals and such other conditions as our compensation committee shall determine. Our compensation committee may grant dividend equivalent rights right to participants that entitle the recipient to receive credits for dividends that would be paid if the recipient held a specified number of shares of common stock.

The compensation committee may grant cash bonuses under the 2014 Plan to participants, subject to the achievement of certain performance goals.

The compensation committee may grant awards of restricted stock, restricted stock units, performance shares or cash-based awards to participants that are intended to qualify as “performance-based compensation” under Section 162(m) of the Code. Such awards will only vest or become payable upon the attainment of performance goals that are established by our compensation committee and related to one or more performance criteria. The performance criteria that could be used with respect to any such awards include: total shareholder return, earnings before interest, taxes, depreciation and amortization, net income (loss) (either before or after interest, taxes, depreciation and/or amortization), changes in the market price of our common stock, economic value-added, funds from operations or similar measure, sales or revenue, acquisitions or strategic transactions, operating income (loss), cash flow (including, but not limited to, operating cash flow and free cash flow), return on capital, assets, equity, or investment, return on sales, gross or net profit levels, productivity, expense, margins, operating efficiency, customer satisfaction, working capital, earnings (loss) per share of common stock, sales or market shares and number of customers, any of which may be measured either in absolute terms or as compared to any incremental increase or as compared to results of a peer group. From and after the time that we become subject to Section 162(m) of the Code, the maximum award that is intended to qualify as “performance-based compensation” under Section 162(m) of the Code that may be made to any one employee during any one calendar year period is shares with respect to a stock-based award and $ with respect to a cash-based award.

The 2014 Plan provides that, upon the effectiveness, of a “sale event,” as defined in the 2014 Plan, the successor entity may assume, continue or substitute for outstanding awards, as appropriately adjusted. To the extent that awards are not assumed or continued or substituted by the successor entity, all awards granted under the 2014 Plan shall terminate. In addition, in connection with the termination of the 2014 Plan upon a sale event, we may make or provide for a cash payment to participants holding options and stock appreciation rights, equal to the difference between the per share cash consideration payable to stockholders in the sale event and the exercise price of the options or stock appreciation rights.

Our board of directors may amend or discontinue the 2014 Plan and our compensation committee may amend or cancel outstanding awards for purposes of satisfying changes in law or any other lawful purpose, including option repricing, but no such action may adversely affect rights under an award without the holder's consent. Certain amendments to the 2014 Plan may require the approval of our stockholders.

No awards may be granted under the 2014 Plan after the date that is ten years from the date of stockholder approval of the 2014 Plan.

Amended and Restated 2014 Management Incentive Plan

The Company adopted the Amended and Restated 2014 Management Incentive Plan, or the MIP, in August 2014, in which certain of our named executive officers participate. Pursuant to the MIP, upon a "change in control" (as defined in the MIP), a bonus pool will be created from the proceeds received in connection with such change in control (ranging from 7 percent to 9.75 percent of transaction proceeds, depending upon the level of transaction proceeds received in the transaction), and each participant is entitled to receive a bonus equal to a certain percentage of such bonus pool. The MIP terminates automatically upon the earliest of (i) March 31, 2015 (unless a change in control has occurred prior to such date), (ii) the closing of our initial public offering, (iii) the closing of a qualified financing, as defined in the MIP, and (iv) the date all amounts to be paid under the MIP following a change in control have been paid. Accordingly, the MIP will automatically terminate upon the closing of this offering in accordance with its terms.

Limitations on Liability and Indemnification Matters

Section 145 of the Delaware General Corporation Law, or the DGCL, authorizes a corporation to indemnify its directors and officers against liabilities arising out of actions, suits and proceedings to which they are made or threatened to be made a party by reason of the fact that they have served or are currently serving as a director or officer to a corporation. The indemnity may cover expenses (including attorneys' fees) judgments, fines and amounts paid in settlement actually and reasonably incurred by the director or officer in connection with any such action, suit or proceeding. Section 145 permits corporations to pay expenses (including attorneys' fees) incurred by directors and officers in advance of the final disposition of such action, suit or proceeding. In addition, Section 145 provides that a corporation has the power to purchase and maintain insurance on behalf of its directors and officers against any liability asserted against them and incurred by them in their capacity as a director or officer, or arising out of their status as such, whether or not the corporation would have the power to indemnify the director or officer against such liability under Section 145.

We have adopted provisions in our certificate of incorporation and bylaws to be in effect upon the closing of this offering that limit or eliminate the personal liability of our directors to the fullest extent permitted by the DGCL, as it now exists or may in the future be amended. Consequently, a director will not be personally liable to us or our stockholders for monetary damages or breach of fiduciary duty as a director, except for liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- any unlawful payments related to dividends or unlawful stock purchases, redemptions or other distributions; or
- any transaction from which the director derived an improper personal benefit.

These limitations of liability do not alter director liability under the federal securities laws and do not affect the availability of equitable remedies such as an injunction or rescission.

In addition, our bylaws provide that:

- we will indemnify our directors, officers and, in the discretion of our board of directors, certain employees to the fullest extent permitted by the DGCL, as it now exists or may in the future be amended; and
- we will advance reasonable expenses, including attorneys' fees, to our directors and, in the discretion of our board of directors, to our officers and certain employees, in connection with legal proceedings relating to their service for or on behalf of us, subject to limited exceptions.

Additionally, each of our directors may have certain rights to indemnification, advancement of expenses and/or insurance provided by their affiliates, which indemnification relates to and might apply to the same proceedings arising out of such director's services as a director referenced herein. Nonetheless, we have agreed in the indemnification agreements that our obligations to those same directors are primary and any obligation of the affiliates of those directors to advance expenses or to provide indemnification for the expenses or liabilities incurred by those directors are secondary.

We also maintain general liability insurance which covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers, including liabilities under the Securities Act.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Other than compensation arrangements, we describe below transactions and series of similar transactions, since January 1, 2011, which includes our last three full fiscal years, to which we were a party or will be a party, in which:

- the amounts involved exceeded or will exceed $120,000; and
- any of our directors, executive officers or holders of more than 5% of our capital stock, or any member of the immediate family of the foregoing persons, had or will have a direct or indirect material interest.

Compensation arrangements for our directors and named executive officers are described elsewhere in this prospectus.

Sales and Purchases of Securities

Equity Financings

In June 2010, we entered into a securities purchase agreement pursuant to which we issued to certain investors shares an aggregate of 9,477,907 of our Series AA Preferred Stock in two separate closings at a price of approximately $1.529 per share, as amended, or the 2010 Series AA Purchase Agreement. In May 2011, we issued to certain investors an additional aggregate of 2,329,464 shares of our Series AA Preferred Stock as a result of our attainment of certain milestones under the 2010 Series AA Purchase Agreement. In June 2011, we issued to certain investors an additional aggregate of 3,651,425 shares of our Series AA Preferred Stock pursuant to an elective extension of the 2010 Series AA Purchase Agreement.

The following table summarizes the participation in the 2010 Series AA Preferred Stock financing by any of our directors, executive officers, holders of more than 5% of our voting securities, or any member of the immediate family of the foregoing persons, since January 1, 2011.

Name	Shares of Series AA Preferred Stock	Aggregate Purchase Price Paid
Devon Park Bioventures, L.P.(1)	1,677,097	$ 2,565,746
Pitango Venture Capital Fund IV L.P.(2)	984,987	$ 1,506,907
Pitango Venture Capital Fund Principals L.P.(2)	21,271	$ 32,541
Care Capital Investments III, LP(3)	989,729	$ 1,514,160
Care Capital Offshore Investments III, LP(3)	16,529	$ 25,297
Rho Management Trust I(4)	294,404	$ 450,400
Rho Ventures IV, L.P.(4)	135,120	$ 206,716
Rho Ventures IV (QP), L.P.(4)	318,105	$ 486,661
Rho Ventures IV GmbH & Co. BETEILIGUNGS KG(4)	331,513	$ 507,172
MedImmune Ventures, Inc.(5)	905,633	$ 1,385,503

(1) Devang V. Kantesaria, a member of our board of directors, is a managing member of Devon Park Associates, LLC, of which Devon Park Bioventures, L.P. is an affiliated fund.
(2) Ittai Harel, a member of our board of directors, is a general partner with Pitango Venture Capital, of which Pitango Venture Capital Fund IV L.P. and Pitango Venture Capital Fund Principals L.P. are affiliated funds.
(3) A.N. “Jerry” Karabelas, a member of our board of directors, is a managing member at Care Capital II, LLC and Care Capital III, LLC, of which Care Capital Investments III, LP and Care Capital Offshore Investments III, LP are affiliated funds.

(4) Martin Vogelbaum, a member of our board of directors, is a Partner at Rho Ventures IV Holdings, LLC, of which Rho Management Trust I, Rho Ventures IV, L.P, Rho Ventures IV (QP), L.P., and Rho Ventures IV GmbH & Co. BETEILIGUNGS KG are affiliated funds.
(5) Isai Peimer, a member of our board of directors, is a Principal of MedImmune Ventures, Inc.

In July 2012, we issued unsecured convertible promissory notes in a private placement for aggregate proceeds of $1.5 million. In November 2012, we issued unsecured convertible promissory notes in a private placement for aggregate proceeds of $1.0 million. In February 2013, we issued unsecured convertible promissory notes in a private placement for aggregate proceeds of $1.0 million. In June 2013, we entered into a securities purchase agreement pursuant to which the promissory notes were converted into 2,677,731 shares of Series AA Preferred Stock in accordance with their terms at a price of $1.3761 per share and we issued to certain investors an additional aggregate of 5,687,991 shares of our Series AA Preferred Stock at a price of $1.529 per share, or the 2013 Series AA Purchase Agreement. In July 2013, we issued an additional aggregate of 852,230 shares of our Series AA Preferred Stock to certain investors and warrants to purchase 852,230 shares of our Series AA Preferred Stock at an exercise price of $0.01 per share, which will terminate upon the closing of this offering, pursuant to the 2013 Series AA Purchase Agreement.

The following table summarizes the participation in the 2013 Series AA Preferred Stock financing by any of our directors, executive officers, holders of more than 5% of our voting securities, or any member of the immediate family of the foregoing persons.

Name	Principal Amount of Convertible Promissory Notes	Shares of Series AA Preferred Stock	Warrants to Purchase Series AA Preferred Stock	Aggregate Purchase Price Paid
Devon Park Bioventures, L.P.(1)	968,789	2,852,631	301,141	$4,248,346.76
Pitango Venture Capital Fund IV L.P.(2)	568,986	988,183	–	$1,444,372.91
Pitango Venture Capital Fund Principals L.P.(2)	12,287	21,319	–	$ 31,161.02
Care Capital Investments III, LP(3)	571,726	1,683,490	177,717	$2,507,174.01
Care Capital Offshore Investments III, LP(3)	9,548	28,115	2,968	$ 41,870.35
Rho Ventures IV Holdings, LLC(4)	182,366	536,983	56,687	$ 799,713.93
Rho Ventures IV, L.P.(4)	83,699	246,453	26,017	$ 367,036.97
Rho Ventures IV (QP), L.P.(4)	197,047	580,211	61,251	$ 864,093.40
Rho Ventures IV GmbH & Co. BETEILIGUNGS KG(4)	205,353	604,668	63,833	$ 900,515.95
MedImmune Ventures, Inc.(5)	523,146	1,540,444	162,616	$2,294,139.87

(1) Devang V. Kantesaria, a member of our board of directors, is a managing member of Devon Park Associates, LLC, of which Devon Park Bioventures, L.P. is an affiliated fund.
(2) Ittai Harel, a member of our board of directors, is a general partner with Pitango Venture Capital, of which Pitango Venture Capital Fund IV L.P. and Pitango Venture Capital Fund Principals L.P. are affiliated funds.
(3) A.N. “Jerry” Karabelas, a member of our board of directors, is a managing member at Care Capital II, LLC and Care Capital III, LLC, of which Care Capital Investments III, LP and Care Capital Offshore Investments III, LP are affiliated funds.
(4) Martin Vogelbaum, a member of our board of directors, is a Partner at Rho Ventures IV Holdings, LLC, of which Rho Ventures IV, L.P, Rho Ventures IV (QP), L.P., and Rho Ventures IV GmbH & Co. BETEILIGUNGS KG are affiliated funds.
(5) Isai Peimer, a member of our board of directors, is a Principal of MedImmune Ventures, Inc.

Agreements With Our Stockholders

In connection with our preferred stock financings, we entered into an investor rights agreement and a stockholders agreement, in each case, with the purchasers of our preferred stock and, in the case of the stockholders agreement, certain holders of our common stock. Our third amended and restated investor rights agreement, or Investor Rights Agreement, provides those certain holders of our preferred stock with the right to demand that we file a registration statement, subject to certain limitations, and to request that their shares be covered by a registration statement that we are otherwise filing. See “Description of Capital Stock—Registration Rights” for additional information.

Our third amended and restated stockholders agreement, as amended, or Stockholders Agreement, provides for rights of first refusal, co-sale and drag along rights in respect of sales by certain holders of our capital stock. The Stockholders Agreement further provides certain holders of our capital stock with a participation right to purchase their *pro rata* share of new securities that we may propose to sell and issue, subject to certain exceptions. Further, the Stockholders Agreement contains provisions with respect to the election of our board of directors and its composition.

The rights under each of the Investor Rights Agreement and the Stockholders Agreement will terminate upon the closing of this offering, other than certain registration rights for certain holders of our preferred stock described below.

Indemnification Agreements

Our Fifth Amended and Restated Certificate of Incorporation and our bylaws, as amended, provide that we shall indemnify our directors and officers to the fullest extent permitted by law. In addition, we have previously entered into and intend to enter into new agreements to indemnify our directors and executive officers. These agreements will, among other things, indemnify these individuals for certain expenses (including attorneys’ fees), judgments, fines and settlement amounts reasonably incurred by such person in any action or proceeding, including any action by or in our right, on account of any services undertaken by such person on behalf of us or that person’s status as a member of our board of directors.

Policies for Approval of Related Party Transactions

Following the closing of this offering, the audit committee of our board of directors will have the primary responsibility for reviewing and approving or disapproving “related party transactions,” which are transactions between us and related persons in which the aggregate amount involved exceeds or may be expected to exceed $120,000 and in which a related person has or will have a direct or indirect material interest. For purposes of this policy, a related person will be defined as a director, executive officer, nominee for director or greater than 5% beneficial owner of our common stock, in each case since the beginning of the most recently completed year, and their immediate family members. Our audit committee charter will provide that the audit committee shall review and approve or disapprove any related party transactions. As of the date of this prospectus, we have not adopted any formal standards, policies or procedures governing the review and approval of related party transactions, but we expect that our audit committee will do so in the future.

All of the transactions described above were entered into prior to the adoption of this policy. Accordingly, each was approved by disinterested members of our board of directors after making a determination that the transaction was executed on terms no less favorable than those that could have been obtained from an unrelated third party.

PRINCIPAL STOCKHOLDERS

The following table sets forth certain information known to us regarding beneficial ownership of our capital stock as of June 30, 2014, as adjusted to reflect the sale of common stock offered by us in this offering, for:

- each person, or group of affiliated persons, known by us to be the beneficial owner of more than 5% of our capital stock;
- our named executive officers;
- each of our other directors; and
- all executive officers and directors as a group.

Beneficial ownership is determined in accordance with the rules of the SEC. A person is deemed to be a beneficial holder of our common stock if that person has or shares voting power, which includes the power to vote or direct the voting of our common stock, or investment power, which includes the power to dispose of or to direct the disposition of such capital stock. Except as noted by footnote, and subject to community property laws where applicable, we believe based on the information provided to us that the persons and entities named in the table below have sole voting and investment power with respect to all common stock shown as beneficially owned by them.

The table lists applicable percentage ownership based on 34,590,552 shares of common stock outstanding as of June 30, 2014, and assumes the conversion of all of our outstanding 25,097,103 shares of preferred stock, including all accrued and unpaid dividends thereon, into 30,450,953 shares of common stock, which will occur immediately prior to the closing of this offering. Shares of common stock that may be acquired by an individual or group within 60 days of June 30, 2014, pursuant to the exercise of options, warrants or other rights, are deemed to be beneficially owned by the persons holding these options for the purpose of computing percentage ownership of that person, but are not treated as outstanding for the purpose of computing any other person's ownership percentage. The column entitled "Percentage of Shares Beneficially Owned— After this Offering (No Exercise of the Underwriters' Option)" is based on shares of our common stock outstanding after this offering, including the shares of our common stock that we are selling in this offering and assumes no exercise of the underwriters' option. The column entitled "Percentage of Shares Beneficially Owned—After this Offering (Full Exercise of the Underwriters' Option)" is based on shares of our common stock outstanding after this offering, including the shares of our common stock that we are selling in this offering and assumes the exercise in full of the underwriter's option to purchase additional shares to cover overallotments.

Unless otherwise noted below, the address of each person listed on the table is c/o Inotek Pharmaceuticals Corporation, 131 Hartwell Avenue, Suite 105, Lexington, MA 02421.

Name and address of beneficial owner	Number of Shares Beneficially Owned Prior to this Offering	Percentage of Shares Beneficially Owned		
		Prior to this Offering	After this Offering (No Exercise of the Underwriters' Option)	After this Offering (Full Exercise of the Underwriters' Option)
5% Stockholders				
Devon Park Bioventures, L.P.(1)	7,432,720	25.2%		
Rho Ventures Entities(2)	6,074,239	20.7%		
Care Capital Entities(3)	5,332,540	18.2%		
MedImmune Ventures, Inc.(4)	4,780,276	16.3%		
Pitango Venture Capital Fund Entities(5)	3,466,213	11.9%		
Named executive officers and directors				
David P. Southwell	0	*		
Rudolf Baumgartner, M.D.(6)	519,452	1.8%		
William K. McVicar, Ph.D.(7)	438,932	1.5%		
Dale Ritter	0	*		
Ittai Harel	0	*		
Paul G Howes(8)	436,830	1.5%		
Devang V. Kantesaria, M.D(1).	7,432,720	25.2%		
A.N. "Jerry" Karabelas, Ph.D.(3)	5,332,540	18.2%		
Isai Peimer(4)	4,780,276	16.3%		
Martin Vogelbaum(2)	0	*		
All directors and executive officers as a group (10 persons)	18,940,750	64.5%		

* Represents beneficial ownership of less than one percent.

(1) Consists of (a) 7,131,579 shares of common stock upon conversion of our outstanding Series AA convertible preferred stock and (b) 301,141 shares of common stock issuable upon the exercise of warrants within 60 days as of June 30, 2014, held by Devon Park Bioventures, L.P. The general partner of Devon Park Bioventures, L.P. is Devon Park Associates, L.P. and Devon Park Associates, LLC is the general partner of Devon Park Associates, L.P. Messrs. Devang V. Kantesaria, a member of our board, Christopher Moller and Marc Ostro are the managing members of Devon Park Associates, LLC. Each such managing director may be deemed to have shared voting and investment power over the shares held by Devon Park Bioventures, L.P. as described above. The address for Devon Park Bioventures, L.P. is 1400 Liberty Ridge Drive, Suite 103, Wayne, Pennsylvania, 19087.

(2) Consists of (a) 1,790,540 shares beneficially owned by Rho Ventures IV (QP), L.P. ("Rho QP"), (b) 1,866,010 shares beneficially owned by Rho Ventures IV GmbH & Co. BETEILIGUNGS KG ("Rho GmbH"), (c) 1,657,132 shares beneficially owned by Rho Ventures IV Holdings LLC ("Rho Holdings"), (d) 338,789 shares beneficially owned by Rho Ventures IV, L.P. ("Rho IV") and (e) 421,768 shares beneficially owned by Rho Ventures IV-A, L.P. ("Rho IV-A"). Rho QP's shares consist of (a) 1,450,530 shares of common stock upon conversion of our outstanding Series AA convertible preferred stock, (b) 278,759 shares of common stock and (c) 61,251 shares of common stock issuable upon the exercise of warrants within 60 days as of June 30, 2014. Rho GmbH's shares consist of (a) 1,511,669 shares of common stock upon conversion of our outstanding Series AA convertible preferred stock, (b) 290,508 shares of common stock and (c) 63,833 shares of common stock issuable upon the exercise of warrants within 60 days as of

June 30, 2014. Rho Holdings' shares consist of (a) 1,342,456 shares of common stock upon conversion of our outstanding Series AA convertible preferred stock, (b) 257,989 shares of common stock and (c) 56,687 shares of common stock issuable upon the exercise of warrants within 60 days as of June 30, 2014. Rho IV's shares consist of (a) 274,457 shares of common stock upon conversion of our outstanding Series AA convertible preferred stock, (b) 52,743 shares of common stock and (c) 11,589 shares of common stock issuable upon the exercise of warrants within 60 days as of June 30, 2014. Rho IV-A's shares consist of (a) 341,677 shares of common stock upon conversion of our outstanding Series AA convertible preferred stock, (b) 65,663 shares of common stock and (c) 14,428 shares of common stock issuable upon the exercise of warrants within 60 days of June 30, 2014. The voting and dispositive decisions with respect to the shares held by Rho IV, Rho Holdings, Rho IV-A, and Rho QP are made by the following managing members of their general partner, Rho Management Ventures IV, L.L.C.: Mark Leschly, Habib Kairouz and Joshua Ruch. The voting and dispositive decisions with respect to the shares held by Rho GmbH are made by the following managing directors of its general partner, Rho Capital Partners Verwaltungs GmbH: Mark Leschly, Habib Kairouz and Joshua Ruch. Martin Vogelbaum, one of our directors, is a non-managing member of Rho Management Ventures IV, L.L.C. and does not have voting or dispositive power with respect to the shares held by Rho QP, Rho GmbH, Rho Holdings, Rho IV or Rho IV-A. The address for the Rho Venture Entities is 152 West 57th Street, 23rd Floor, New York, New York 10019.

(3) Consists of (a) 2,277,674 shares beneficially owned by Care Capital Investments II, LP ("Investments II"), (b) 2,850,936 shares beneficially owned by Care Capital Investments III, L.P. ("Investments III"), (c) 156,318 shares beneficially owned by Care Capital Offshore Investments II, LP ("Offshore II") and (d) 47,612 shares beneficially owned by Care Capital Offshore Investments III, LP ("Offshore III"). Investments II's shares consist of (a) 1,460,829 shares of common stock upon conversion of our outstanding Series AA convertible preferred stock and (b) 816,845 shares of common stock. Investments III's shares consist of (a) 2,673,219 shares of common stock upon conversion of our outstanding Series AA convertible preferred stock and (b) 177,717 shares of common stock issuable upon the exercise of warrants within 60 days as of June 30, 2014. Offshore II's shares consist of (a) 100,281 shares of common stock upon conversion of our outstanding Series AA convertible preferred stock and (b) 56,037 shares of common stock. Offshore III's shares consist of 44,644 shares of common stock upon conversion of our outstanding Series AA convertible preferred stock and (b) 2,968 shares of common stock issuable upon the exercise of warrants within 60 days as of June 30, 2014. The voting and disposition of the shares held by Investments II and Offshore II is determined by the following managing members of their general partner, Care Capital II, LLC: A.N. "Jerry" Karabelas, Ph.D., a member of our Board of Directors, Jan Leschly and David R. Ramsay. The voting and disposition of the shares held by Investments III and Offshore III is determined by the following managing members of their general partner, Care Capital III, LLC: A.N. "Jerry" Karabelas, Ph.D., a member of our Board of Directors, Jan Leschly, Richard Markham and David R. Ramsay. The address of the Care Capital Entities is 47 Hull Street, Suite 310, Princeton, New Jersey 08540.

(4) Consists of (a) 3,851,076 shares of common stock upon conversion of our outstanding Series AA convertible preferred stock, (b) 766,584 shares of common stock and (c) 162,616 shares of common stock issuable upon the exercise of warrants within 60 days of June 30, 2014. Isai Peimer, a member of our Board of Directors, is a Principal of MedImmune Ventures, Inc. The address of MedImmune Ventures, Inc. is 1 MedImmune Way, Gaithersburg, Maryland 20878.

(5) Consists of (a) 3,392,964 shares beneficially owned by Pitango Venture Capital Fund IV L.P. ("Pitango Fund IV") and 73,249 shares beneficially owned by Pitango Venture Capital Fund Principals IV L.P. ("Pitango Principals"). Pitango Fund IV's shares consist of (a) 2,619,795 shares of common stock upon conversion of our outstanding Series AA convertible preferred stock and (b) 773,169 shares of common stock. Pitango Principals' shares consist of (a) 56,553 shares of common stock upon conversion of our outstanding Series AA convertible preferred stock and

(b) 16,696 shares of common stock. The general partner and manager of Pitango Fund IV and Pitango Principals is Pitango V.C. Fund IV, L.P., whose general partner is Pitango G.P. Capital Holdings Ltd., an Israeli company owned indirectly (through personal holding entities) by each of the following individuals: Rami Kalish, Chemi J. Peres, Aaron Mankovski, Isaac Hillel, Rami Beracha and Zeev Binman. These individuals share voting and dispositive power, but none of them has sole voting or dispositive power, over the shares held by Pitango Fund IV and Pitango Principals. Ittai Harel, a member of our Board of Directors, is a general partner with Pitango Venture Capital. The address of the Pitango Fund IV and Pitango Principals is 11 Hamenofim Street, Building B, Herzliya Pituach 46725, Israel.

(6) Consists of (a) 509,837 shares of common stock upon conversion of our outstanding Series X convertible preferred stock and (b) 9,615 shares of common stock issuable upon the exercise of options exercisable within 60 days after June 30, 2014.

(7) Consists of (a) 431,432 shares of common stock upon conversion of our outstanding Series X convertible preferred stock and (b) 7,500 shares of common stock issuable upon the exercise of options exercisable within 60 days after June 30, 2014.

(8) Consists of (a) 411,830 shares of common stock upon conversion of our outstanding Series X convertible preferred stock and (b) 25,000 shares of common stock issuable upon the exercise of options exercisable within 60 days after June 30, 2014.

DESCRIPTION OF CAPITAL STOCK

The following descriptions are summaries of the material terms of our amended and restated certificate of incorporation and amended and restated bylaws, which will be effective upon closing of this offering. The descriptions of the common stock and preferred stock give effect to changes to our capital structure that will occur immediately prior to the closing of this offering. We refer in this section to our amended and restated certificate of incorporation as our certificate of incorporation, and we refer to our amended and restated bylaws as our bylaws.

General

Upon the closing of this offering, our authorized capital stock will consist of shares of common stock, par value $0.01 per share, and shares of preferred stock, par value $0.001 per share, all of which shares of preferred stock will be undesignated.

As of June 30, 2014, 4,139,599 shares of our common stock were outstanding and held by 34 stockholders of record. In addition, as of June 30, 2014, 25,097,103 shares of preferred stock were outstanding and, with all accrued and unpaid dividends thereon, will convert into 30,450,953 shares of common stock upon the closing of this offering. Further, as of June 30, 2014, we had outstanding options to purchase 48,137 shares of our common stock, at a weighted average exercise price of $10.00 per share, all of which were exercisable and outstanding.

Common Stock

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by the board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock. The shares to be issued by us in this offering will be, when issued and paid for, validly issued, fully paid and non-assessable.

Preferred Stock

Immediately prior to the closing of this offering, all outstanding shares of our preferred stock, including all accrued and unpaid dividends thereon, will be converted into shares of our common stock. Immediately prior to the closing of this offering, our Fifth Amended and Restated Certificate of Incorporation will be amended and restated to, among other things, delete all references to such shares of preferred stock. Upon the closing of this offering, our board of directors will have the authority, without further action by our stockholders, to issue up to shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action. Immediately after closing of this offering, no shares of preferred stock will be outstanding, and we have no present plans to issue any shares of preferred stock.

Warrants

As of June 30, 2014, we had the following outstanding warrants to purchase shares of our Series AA Preferred Stock:

Number of Underlying Shares	Exercise Price Per Share	Warrant Expiration Date
177,717	$0.01	July 11, 2023(1)
2,968	$0.01	July 11, 2023(1)
301,141	$0.01	July 11, 2023(1)
162,616	$0.01	July 11, 2023(1)
61,251	$0.01	July 11, 2023(1)
63,833	$0.01	July 11, 2023(1)
56,687	$0.01	July 11, 2023(1)
14,428	$0.01	July 11, 2023(1)
11,589	$0.01	July 11, 2023(1)
114,453	$1.529	June 28, 2023(2)
114,453	$1.529	June 28, 2023(2)

(1) Warrants automatically terminate upon the closing of this offering if it occurs prior to the expiration date.
(2) Warrants automatically terminate upon the closing of a sale or lease of all or substantially all of our business or property, our merger into or consolidation with any other corporation other than a wholly owned subsidiary of ours or any transaction or series of transactions pursuant to which more than 50% of the voting power of our capital stock is transferred.

Upon the closing of this offering, each of our warrants that does not automatically terminate upon the closing of this offering will become exercisable for shares of our common stock rather than Series AA Preferred Stock. The number of shares of our common stock into which the warrant will become exercisable will equal the number of shares of our common stock that the holder would have received if the warrant had been exercised in full and the resulting shares of convertible preferred stock received had been converted into shares of our common stock.

Registration Rights

Upon the closing of this offering, the holders of our registrable shares, as described in the Investor Rights Agreement, are entitled to rights with respect to the registration of these shares under the Securities Act as hereinafter described. These rights are provided under the terms of the Investor Rights Agreement, and include demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs and expenses of underwritten registrations will be borne by us and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

Demand Registration Rights

Upon the closing of this offering, certain holders of shares of our common stock, including shares issuable upon the conversion of preferred stock or their permitted transferees, are entitled to demand registration rights. Under the terms of the Investor Rights Agreement, we will be required, upon the written request of holders of at least 50% of our common shares issued upon conversion of our preferred stock upon consummation of this offering, to register shares with an anticipated aggregate offering price of at least $5,000,000, to use our commercially reasonable efforts to effect the registration of at least 25% of our common shares issued upon conversion of our preferred stock upon consummation of this offering, subject to certain exceptions. We are required to effect only two registrations pursuant to this provision of the Investor Rights Agreement. A demand for registration may not be made until 180 days after the closing of this offering.

Form S-3 Registration Rights

Upon the closing of this offering, certain holders of shares of our common stock issued upon the conversion of preferred stock or their permitted transferees are also entitled to short form registration rights. If we are eligible to file a registration statement on Form S-3, upon the written request of certain holders of our common stock issued upon conversion of our preferred stock upon consummation of this offering to register shares with an anticipated aggregate offering price of at least $1,000,000, we will be required to use our best efforts to effect a registration of such shares, subject to certain exceptions.

Piggyback Registration Rights

Upon the closing of this offering, certain holders of shares of our common stock issued upon the conversion of preferred stock or their permitted transferees are entitled to piggyback registration rights. If we propose to register any of our securities either for our own account or for the account of other security holders, the holders of these shares are entitled to include their shares in the registration. Subject to certain exceptions, we and the underwriters may limit the number of shares included in the underwritten offering if the underwriters believe that including these shares would adversely affect the offering.

Indemnification

Our Investor Rights Agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of Registration Rights

The registration rights granted under the Investor Rights Agreement will terminate on the fifth anniversary of the closing of this offering.

Anti-takeover Effects of Our Certificate of Incorporation, Bylaws and Delaware Law

Our certificate of incorporation and bylaws that will be effective upon consummation of this offering include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board Composition and Filling Vacancies

Our certificate of incorporation provides for the division of our board of directors into three classes serving staggered three-year terms, with one class being elected each year. Our certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of 75% of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum. The classification of directors, together with the limitations on removal of directors and treatment of vacancies, has the effect of making it more difficult for stockholders to change the composition of our board of directors.

No Written Consent of Stockholders

Our certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our bylaws or removal of directors by our stockholders without holding a meeting of stockholders.

Meetings of Stockholders

Our certificate of incorporation and bylaws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance Notice Requirements

Our bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our bylaws specify the requirements as to form and content of all stockholders' notices. These requirements may preclude stockholders from bringing matters before the stockholders at an annual or special meeting.

Amendment to Certificate of Incorporation and Bylaws

Any amendment of our certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, limitation of liability and the amendment of our certificate of incorporation must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the bylaws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment, or, if our board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Undesignated Preferred Stock

Our certificate of incorporation provides for authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Section 203 of the Delaware General Corporation Law

Upon the closing of this offering, we will be subject to the provisions of Section 203 of the DGCL. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this

stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

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

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

Exchange Listing

We intend to apply to list our common stock on The NASDAQ Global Market under the trading symbol “ITEK.”

Transfer Agent and Registrar

The transfer agent and registrar for our common stock will be . The transfer agent and registrar’s address is .

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our shares. Future sales of our common stock in the public market, or the availability of such shares for sale in the public market, could adversely affect market prices prevailing from time to time. As described below, only a limited number of shares will be available for sale shortly after this offering due to contractual and legal restrictions on resale. Nevertheless, sales of our common stock in the public market after such restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price at such time and our ability to raise equity capital in the future.

Based on the number of shares outstanding as of June 30, 2014, upon the closing of this offering, shares of our common stock will be outstanding, assuming no exercise of the underwriters' over-allotment option to purchase additional shares and no exercise of outstanding options. Of the outstanding shares, all of the shares sold in this offering will be freely tradable, except that any shares held by our affiliates, as that term is defined in Rule 144 under the Securities Act, may only be sold in compliance with the limitations described below.

Rule 144

In general, a person who has beneficially owned restricted stock for at least six months would be entitled to sell their securities provided that (i) such person is not deemed to have been one of our affiliates at the time of, or at any time during the 90 days preceding, a sale and (ii) we are subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale. Persons who have beneficially owned restricted shares for at least six months but who are our affiliates at the time of, or any time during the 90 days preceding, a sale, would be subject to additional restrictions, by which such person would be entitled to sell within any three-month period only a number of securities that does not exceed the greater of either of the following:

- 1% of the number of shares then outstanding, which will equal approximately shares immediately after this offering assuming no exercise of the underwriters' option to purchase additional shares, based on the number of shares outstanding as of June 30, 2014; or
- the average weekly trading volume of our common stock on during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale.

Provided, in each case, that we are subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale. Such sales both by affiliates and by non-affiliates must also comply with the manner of sale, current public information and notice provisions of Rule 144.

Rule 701

Rule 701 under the Securities Act, as in effect on the date of this prospectus, permits resales of shares in reliance upon Rule 144 but without compliance with certain restrictions of Rule 144, including the holding period requirement. Most of our employees, executive officers or directors who purchased shares under a written compensatory plan or contract may be entitled to rely on the resale provisions of Rule 701, but all holders of Rule 701 shares are required to wait until 90 days after the date of this prospectus before selling their shares. However, substantially all Rule 701 shares are subject to lock-up agreements as described below and under "Underwriting" included elsewhere in this prospectus and will become eligible for sale upon the expiration of the restrictions set forth in those agreements.

Lock-up Agreements

In connection with this offering, all of our directors and executive officers and certain holders of our shares, who collectively held shares of common stock (assuming conversion of all of our outstanding shares of preferred stock) as of June 30, 2014, and substantially all of our optionholders who are not stockholders, have signed lock-up agreements which prevent them from selling any of our common stock or any securities convertible into or exercisable or exchangeable for common stock for a period of not less than 180 days from the date of the preliminary prospectus prepared for this offering without the prior written consent of each of Cowen and Company, LLC and Piper Jaffray & Co., as representatives of the underwriters. The representatives may in their sole discretion and at any time without notice release some or all of the shares subject to lock-up agreements prior to the expiration of the 180-day period. When determining whether or not to release shares from the lock-up agreements, the representatives will consider, among other factors, the stockholder's reasons for requesting the release, the number of shares for which the release is being requested and market conditions at the time. In addition, our optionholders who have not executed lock-up agreements are nevertheless subject to similar restrictions set forth in the option agreements executed in connection with our 2004 Plan and 2014 Plan.

Registration Rights

Upon the closing of this offering, the holders of shares of common stock or their transferees will be entitled to various rights with respect to registration of these shares under the Securities Act. Registration of these shares under the Securities Act would result in these shares becoming fully tradable without restriction under the Securities Act immediately upon the effectiveness of the registration. See "Description of Capital Stock—Registration Rights" for additional information.

Stock Option Plans

We intend to file one or more registration statements on Form S-8 under the Securities Act to register our shares issued or reserved for issuance under the 2014 Plan. The first such registration statement is expected to be filed soon after the date of this prospectus and will automatically become effective upon filing with the SEC. Accordingly, shares registered under such registration statement will be available for sale in the open market, unless such shares are subject to vesting restrictions with us or the lock-up restrictions described above. We estimate that such registration statement on Form S-8 will cover approximately shares.

CERTAIN MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF COMMON STOCK

The following is a general discussion of the material U.S. federal income and estate tax considerations applicable to non-U.S. holders (as defined below) with respect to their ownership and disposition of shares of our common stock issued pursuant to this offering. For purposes of this discussion, a non-U.S. holder means a beneficial owner of our common stock that is for U.S. federal income tax purposes

- a non-resident alien individual;
- a foreign corporation or any other organization taxable as a corporation for U.S. federal income tax purposes or;
- a foreign estate or trust, the income of which is not subject to U.S. federal income tax on a net-income basis.

This discussion does not address the tax treatment of partnerships or other entities that are pass-through entities for U.S. federal income tax purposes or persons that hold their common stock through partnerships or other pass-through entities. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its own tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus, all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change could alter the tax consequences to non-U.S. holders described in this prospectus. There can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described herein. We assume in this discussion that a non-U.S. holder holds shares of our common stock as a capital asset, generally property held for investment.

This discussion does not address all aspects of U.S. federal income and estate taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address any aspects of U.S. state, local or non-U.S. taxes, the alternative minimum tax, or the Medicare tax on net investment income. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- insurance companies;
- tax-exempt organizations;
- financial institutions;
- brokers or dealers in securities;
- regulated investment companies;
- pension plans;
- controlled foreign corporations;
- passive foreign investment companies;
- persons that have a functional currency other than the U.S. dollar;
- owners deemed to sell our common stock under the constructive sale provisions of the Code;
- owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment; and
- certain U.S. expatriates.

This discussion is for general information only and is not tax advice. Accordingly, all prospective non-U.S. holders of our common stock should consult their own tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock.

Distributions on Our Common Stock

Distributions, if any, on our common stock generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in "Gain on sale, exchange or other disposition of our common stock." Any such distributions will also be subject to the discussion below under the section titled "Withholding and Information Reporting Requirements—FATCA."

Dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing a U.S. tax return with the IRS.

Gain on Sale, Exchange or Other Disposition of Our Common Stock

In general, a non-U.S. holder will not be subject to any U.S. federal income tax on any gain realized upon such holder's sale, exchange or other disposition of shares of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a U.S. trade or business and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed-base maintained by such non-U.S. holder in the United States, in which case the non-U.S. holder generally will be taxed on a net income basis at the graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in "Distributions on Our Common Stock" also may apply;

- the non-U.S. holder is a nonresident alien individual who is present in the United States for 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) on the net gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder, if any (even though the individual is not considered a resident of the United States, provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses); or
- we are, or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation," unless our common stock is regularly traded on an established securities market and the non-U.S. holder holds no more than 5% of our outstanding common stock, directly or indirectly, actually or constructively, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. If we are determined to be a U.S. real property holding corporation and the foregoing exception does not apply, then a purchaser may withhold 10% of the proceeds payable to a non-U.S. holder from a sale of our common stock and the non-U.S. holder generally will be taxed on its net gain derived from the disposition at the graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code). Generally, a corporation is a U.S. real property holding corporation only if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

U.S. Federal Estate Tax

Shares of our common stock that are owned or treated as owned at the time of death by an individual who is not a citizen or resident of the United States, as specifically defined for U.S. federal estate tax purposes, are considered U.S. situs assets and will be included in the individual's gross estate for U.S. federal estate tax purposes. Such shares, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

Backup Withholding and Information Reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a United States person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above in "Distributions on Our Common Stock," generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with

substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is filed with the IRS in a timely manner.

Withholding and Information Reporting Requirements—FATCA

The Foreign Account Tax Compliance Act, or FATCA, generally imposes a U.S. federal withholding tax at a rate of 30% on payments of dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a foreign entity unless (i) if the foreign entity is a "foreign financial institution," such foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a "foreign financial institution," such foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA. Under applicable U.S. Treasury regulations, withholding under FATCA will apply to payments of dividends on our common stock made after June 30, 2014, but will only apply to payments of gross proceeds from a sale or other disposition of our common stock made after December 31, 2016. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of the tax. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph. Non-U.S. holders should consult their own tax advisors regarding the possible implications of this legislation on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

UNDERWRITING

We and the underwriters for the offering named below have entered into an underwriting agreement with respect to the shares of common stock being offered. Subject to the terms and conditions of the underwriting agreement, each underwriter has severally agreed to purchase from us the number of shares of common stock set forth opposite its name below. Cowen and Company, LLC and Piper Jaffray & Co. are the representatives of the underwriters.

Underwriter	Number of Shares
Cowen and Company, LLC	
Piper Jaffray & Co.	
Total	

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent and that the underwriters have agreed, severally and not jointly, to purchase all of the shares of common stock sold under the underwriting agreement if any of these shares are purchased, other than those shares covered by the overallotment option described below. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against specified liabilities, including liabilities under the Securities Act, and to contribute to payments the underwriters may be required to make in respect thereof.

The underwriters are offering the shares of common stock, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel and other conditions specified in the underwriting agreement. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Overallotment Option to Purchase Additional Shares

We have granted to the underwriters an option to purchase up to additional shares of common stock at the public offering price, less the underwriting discount. This option is exercisable for a period of 30 days. The underwriters may exercise this option solely for the purpose of covering overallotments, if any, made in connection with the sale of common stock offered hereby. To the extent that the underwriters exercise this option, the underwriters will purchase additional shares from us in approximately the same proportion as shown in the table above.

Discounts and Commissions

The following table shows the public offering price, underwriting discount and proceeds, before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares of common stock.

We estimate that the total expenses of the offering, excluding underwriting discount, will be approximately $ and are payable by us.

		Total	
	Per Share	Without Over-Allotment	With Over Allotment
Initial public offering price			
Underwriting discounts and commissions			
Proceeds, before expenses, to Inotek			

The underwriters propose to offer the shares of common stock to the public at the public offering price set forth on the cover of this prospectus. The underwriters may offer the shares of common stock to securities dealers at the public offering price less a concession not in excess of $ per share. If all of the shares are not sold at the public offering price, the underwriters may change the offering price and other selling terms.

Discretionary Accounts

The underwriters do not intend to confirm sales of the shares of common stock to any accounts over which they have discretionary authority.

Market Information

Prior to this offering, there has been no public market for shares of our common stock. The initial public offering price will be determined by negotiations between us and the representatives of the underwriters. In addition to prevailing market conditions, the factors to be considered in these negotiations include:

- the history of, and prospects for, our company and the industry in which we compete;
- our past and present financial information;
- an assessment of our management; its past and present operations, and the prospects for, and timing of, our future revenues;
- the present state of our development; and
- the above factors in relation to market values and various valuation measures of other companies engaged in activities similar to ours.

An active trading market for our common stock may not develop, of if such a market develops, may not be sustained. It is also possible that after the offering the shares will not trade in the public market at or above the initial public offering price.

We intend to apply to list our common stock on the NASDAQ Global Market under the symbol ‘‘ITEK.’’

Price Stabilization, Short Positions and Penalty Bids

In connection with this offering, the underwriters may engage in stabilizing transactions, overallotment transactions, syndicate covering transactions, penalty bids and purchases to cover positions created by short sales.

- Stabilizing transactions permit bids to purchase shares of common stock so long as the stabilizing bids do not exceed a specified maximum, and are engaged in for the purpose of preventing or retarding a decline in the market price of the common stock while the offering is in progress.
- Overallotment transactions involve sales by the underwriters of shares of common stock in excess of the number of shares the underwriters are obligated to purchase. This creates a syndicate short position which may be either a covered short position or a naked short position. In a covered short position, the number of shares over-allotted by the underwriters is not greater than the number of shares that they may purchase in the overallotment option. In a naked short position, the number of shares involved is greater than the number of shares in the overallotment option. The underwriters may close out any short position by exercising their overallotment option and/or purchasing shares in the open market.
- Syndicate covering transactions involve purchases of common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining

the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared with the price at which they may purchase shares through exercise of the overallotment option. If the underwriters sell more shares than could be covered by exercise of the overallotment option and, therefore, have a naked short position, the position can be closed out only by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that after pricing there could be downward pressure on the price of the shares in the open market that could adversely affect investors who purchase in the offering.

- Penalty bids permit the representatives to reclaim a selling concession from a syndicate member when the common stock originally sold by that syndicate member is purchased in stabilizing or syndicate covering transactions to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock in the open market may be higher than it would otherwise be in the absence of these transactions. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of shares of our common stock. These transactions may be effected on the NASDAQ Global Market, in the over-the-counter market or otherwise and, if commenced, may be discontinued at any time.

Lock-Up Agreements

Pursuant to certain ‘‘lock-up’’ agreements, we and our executive officers, directors and certain of our other stockholders, have agreed, subject to certain exceptions, not to offer, sell, assign, transfer, pledge, contract to sell, or otherwise dispose of or announce the intention to otherwise dispose of, or enter into any swap, hedge or similar agreement or arrangement that transfers, in whole or in part, the economic consequence of ownership of, directly or indirectly, or make any demand or request or exercise any right with respect to the registration of, or file with the SEC a registration statement under the Securities Act relating to, any common stock or securities convertible into or exchangeable or exercisable for any common stock without the prior written consent of Cowen and Company, LLC and Piper Jaffray & Co., for a period of 180 days after the date of the underwriting agreement.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition. The exceptions to the lock-up for executive officers, directors and stockholders include: (a) transfers made as a bona fide gift to an immediate family member, to a trust the beneficiaries of which are exclusively the executive officer, director or stockholder or immediate family member, or to a charity or educational institution; (b) transfers made by will or intestate succession; (c) transfers not for value to a stockholder, partner, member or similar equity owner of, or business entity that is an affiliate of, a similar equity interest in, a stockholder that is an entity; (d) transfers made by an employee or director pursuant to a net exercise or cashless exercise of outstanding equity awards pursuant to our equity plans or as forfeitures or sales to us of common stock or securities convertible into common stock to cover tax withholding obligations in connection with the vesting, settlement or exercise of equity awards outstanding on the date of the underwriting agreement; (e) the conversion, exchange or exercise of any securities convertible into or exchangeable for our common stock; (f) transactions relating to our common stock or other securities convertible into or exercisable or exchangeable for our common stock acquired in open market transactions after the date of this prospectus, provided that no such transaction is required to be, or is, publicly announced; (g) transactions relating to our common stock acquired through our initial public offering, provided that

no such transaction is required to be, or is, publicly announced, and provided further that this sub-clause will not apply to our officers and directors; (h) the establishment of a trading plan in accordance with Rule 10b5-l(c) under the Exchange Act, provided that no sale or other disposition under such trading plan may occur during the 180-day restricted period; and (i) transfers pursuant to a bona fide third party tender offer, merger, consolidation or other similar transaction made to holders of our common stock involving the transfer in one or more transactions to a person or affiliated persons of our voting securities if, after such transfer, such person or group of affiliated persons would hold 90% of our outstanding voting securities. The exceptions to the lock-up for us are: (i) our sale of shares in this offering; (ii) the issuance of common stock or options to acquire common stock pursuant to our employee benefit plans, equity compensation plans or other compensation plans in existence on the date hereof and as described in this prospectus; and (iii) the issuance of common stock pursuant to the conversion or exercise of existing securities. In addition, the lock-up provision will not restrict broker-dealers from engaging in market making and similar activities conducted in the ordinary course of their business.

Cowen and Company, LLC and Piper Jaffray & Co., in their sole discretion, may release our common stock and other securities subject to the lock-up agreements described above in whole or in part at any time. When determining whether or not to release our common stock and other securities from lock-up agreements, Cowen and Company, LLC and Piper Jaffray & Co. will consider, among other factors, the holder's reasons for requesting the release, the number of shares for which the release is being requested and market conditions at the time of the request. In the event of such a release or waiver for one of our directors or officers, Cowen and Company, LLC and Piper Jaffray & Co. shall provide us with notice of the impending release or waiver at least three business days before the effective date of such release or waiver and we will announce the impending release or waiver by issuing a press release at least two business days before the effective date of the release or waiver.

Electronic Offer, Sale and Distribution of Shares

A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters or selling group members, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute prospectuses electronically. The representatives may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters and selling group members that will make internet distributions on the same basis as other allocations. Other than the prospectus in electronic format, the information on these websites is not part of this prospectus or the registration statement of which this prospectus forms a part, has not been approved or endorsed by us or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

Other Relationships

Certain of the underwriters and their affiliates have provided, and may in the future provide, various investment banking, commercial banking and other financial services for us and our affiliates for which they have received, and may in the future receive, customary fees.

Selling Restrictions

No action has been taken in any jurisdiction except the United States that would permit a public offering of our common stock, or the possession, circulation or distribution of this prospectus or any other material relating to us or our common stock in any jurisdiction where action for that purpose is required. Accordingly, the shares may not be offered or sold, directly or indirectly, and neither this prospectus nor any other offering material or advertisements in connection with the shares may be distributed or published, in or from any country or jurisdiction except in compliance with any applicable rules and regulations of any such country or jurisdiction.

United Kingdom

Each of the underwriters has, separately and not jointly, represented and agreed that:

- it has not made or will not make an offer of the securities to the public in the United Kingdom within the meaning of section 102B of the Financial Services and Markets Act 2000 (as amended), or the FSMA, except to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities or otherwise in circumstances which do not require the publication by us of a prospectus pursuant to the Prospectus Rules of the Financial Services Authority, or FSA;
- it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of section 21 of FSMA) to persons who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 or in circumstances in which section 21 of FSMA does not apply to us; and
- it has complied with and will comply with all applicable provisions of FSMA with respect to anything done by it in relation to the securities in, from or otherwise involving the United Kingdom.

Switzerland

The securities will not be offered, directly or indirectly, to the public in Switzerland and this prospectus does not constitute a public offering prospectus as that term is understood pursuant to article 652a or 1156 of the Swiss Federal Code of Obligations.

European Economic Area

In relation to each Member State of the European Economic Area, or the EEA, which has implemented the European Prospectus Directive (each, a “Relevant Member State”), an offer of our shares may not be made to the public in a Relevant Member State other than:

- to any legal entity which is a qualified investor, as defined in the European Prospectus Directive;
- to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the European Prospectus Directive), subject to obtaining the prior consent of the relevant dealer or dealers nominated by us for any such offer, or
- in any other circumstances falling within Article 3(2) of the European Prospectus Directive,

provided that no such offer of our shares shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the European Prospectus Directive or supplement prospectus pursuant to Article 16 of the European Prospectus Directive.

For the purposes of this description, the expression an “offer to the public” in relation to the securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe for the securities, as the expression may be varied in that Relevant Member State by any measure implementing the European Prospectus Directive in that member state, and the expression “European Prospectus Directive” means Directive 2003/71/EC (and amendments hereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State) and includes any relevant implementing measure in each Relevant Member State. The expression 2010 PD Amending Directive means Directive 2010/73/EU.

We have not authorized and do not authorize the making of any offer of securities through any financial intermediary on our behalf, other than offers made by the underwriters and their respective affiliates, with a view to the final placement of the securities as contemplated in this document. Accordingly, no purchaser of the shares, other than the underwriters, is authorized to make any further offer of shares on our behalf or on behalf of the underwriters.

LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Certain legal matters will be passed upon for the underwriters by Cooley LLP, New York, New York.

EXPERTS

The consolidated financial statements of Inotek Pharmaceuticals Corporation appearing in this prospectus and registration statement have been audited by McGladrey LLP, an independent registered public accounting firm, as stated in their report appearing elsewhere herein, and are included in reliance upon such report and upon the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 (File Number 333-) under the Securities Act with respect to the common stock we are offering by this prospectus. This prospectus does not contain all of the information included in the registration statement. For further information pertaining to us and our common stock, you should refer to the registration statement and to its exhibits. Whenever we make reference in this prospectus to any of our contracts, agreements or other documents, the references are not necessarily complete, and you should refer to the exhibits attached to the registration statement for copies of the actual contract, agreement or other document.

Upon the closing of the offering, we will be subject to the informational requirements of the Exchange Act and will file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, over the Internet at the SEC's website at www.sec.gov. You may also read and copy any document we file with the SEC at its public reference facility at 100 F Street, N.E., Room 1580, Washington, D.C. 20549.

You may also obtain copies of the documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facilities.

Inotek Pharmaceuticals Corporation

Index to Consolidated Financial Statements

Contents

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders
Inotek Pharmaceuticals Corporation

We have audited the accompanying consolidated balance sheets of Inotek Pharmaceuticals Corporation as of December 31, 2013 and 2012, and the related consolidated statements of operations, changes in redeemable convertible preferred stock and stockholders' deficit, and cash flows for the years then ended. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of Inotek Pharmaceuticals Corporation as of December 31, 2013 and 2012, and the results of their operations and their cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

/s/ McGladrey LLP

Boston, Massachusetts
August 29, 2014

Inotek Pharmaceuticals Corporation

Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31, 2012	December 31, 2013	June 30, 2014 (unaudited)	Pro Forma June 30, 2014 (unaudited)
Assets				
Current assets:				
Cash and cash equivalents	$ 1,372	$ 12,793	$ 8,881	$ 8,881
Prepaid expenses and other current assets	45	66	38	38
Total current assets	1,417	12,859	8,919	8,919
Other assets	4	4	4	4
Total assets	$ 1,421	$ 12,863	$ 8,923	$ 8,923
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Deficit				
Current liabilities				
Notes payable-current portion	$ –	$ 1,410	$ 2,899	$ 2,899
Accounts payable	387	229	357	357
Accrued expenses and other current liabilities	665	1,579	1,798	1,798
Convertible notes payable	2,713	–	–	–
Total current liabilities	3,765	3,218	5,054	5,054
Notes payable, net of current portion	–	5,395	4,012	4,012
Warrant liabilities	–	1,888	2,486	–
Other long-term liabilities	24	24	24	24
Total liabilities	3,789	10,525	11,576	9,090
Series AA redeemable convertible preferred stock, $0.001 par value; 25,757,874 shares authorized; 15,458,796 issued and outstanding at December 31, 2012, 23,204,783 shares issued and outstanding at December 31, 2013 and June 30, 2014 (unaudited) and no shares issued and outstanding pro forma (unaudited); (liquidation preference of $96,886 at June 30, 2014 (unaudited), See Note 7)	27,856	40,685	42,715	–
Series X redeemable convertible preferred stock, $0.001 par value; 2,902,050 shares authorized; 2,451,184 shares issued and outstanding at December 31, 2012, 1,892,320 shares issued and outstanding at December 31, 2013 and June 30, 2014 (unaudited) and no shares issued and outstanding pro forma (unaudited); (liquidation preference, see Note 7)	706	548	548	–
Total redeemable convertible preferred stock	28,562	41,233	43,263	–
Commitments and Contingencies (Note 8)				
Stockholders' deficit:				
Common stock, $0.01 par value; 32,857,171 shares authorized; 4,132,530 shares issued and 4,124,880 shares outstanding at December 31, 2012, 4,147,249 shares issued and 4,139,599 shares outstanding at December 31, 2013 and June 30, 2014 and 34,598,202 shares issued and 34,590,552 shares outstanding pro forma (unaudited)	41	41	41	346
Treasury stock, at cost 7,650 shares, at December 31, 2012 and 2013 and at June 30, 2014 (unaudited)	(176)	(176)	(176)	(176)
Additional paid-in capital	80,099	79,750	77,724	123,168
Accumulated deficit	(110,894)	(118,510)	(123,505)	(123,505)
Total stockholders' deficit	(30,930)	(38,895)	(45,916)	(167)
Total Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Deficit	$ 1,421	$ 12,863	$ 8,923	$ 8,923

The accompanying notes are an integral part of these consolidated financial statements.

Inotek Pharmaceuticals Corporation

Consolidated Statements of Operations
(in thousands, except share and per share amounts)

	Year ended December 31,		Six months ended June 30,	
	2012	2013	2013	2014
			(unaudited)	
Operating expenses:				
Research and development	$ (3,542)	$ (5,330)	$ (2,304)	$ (3,412)
General and administrative	(2,307)	(1,324)	(1,021)	(494)
Loss from operations	(5,849)	(6,654)	(3,325)	(3,906)
Other income	4	3	–	–
Interest expense	(213)	(884)	(388)	(491)
Change in fair value of warrant liabilities	–	(81)	–	(598)
Net loss	$ (6,058)	$ (7,616)	$ (3,713)	$ (4,995)
Net loss per share attributable to common stockholders—basic and diluted	$ (1.98)	$ (2.48)	$ (1.18)	$ (1.70)
Weighted-average number of shares outstanding—basic and diluted	4,124,880	4,131,863	4,124,880	4,139,599
Pro forma net loss per share attributable to common stockholders—basic and diluted (unaudited)		$ (0.35)		$ (0.21)
Pro forma weighted-average number of shares outstanding—basic and diluted (unaudited)		29,413,014		33,796,398

The accompanying notes are an integral part of these consolidated financial statements.

Inotek Pharmaceuticals Corporation

Consolidated Statements of Changes in Redeemable Convertible Preferred Stock and Stockholders' Deficit
(in thousands, except share and per share data)

	Series AA Redeemable Convertible Preferred Stock		Series X Redeemable Convertible Preferred Stock		Common Stock		Treasury Stock		Additional Paid-In Capital	Accumulated Deficit	Total
	Shares	Amount	Shares	Amount	Shares	Par Value	Shares	Amount			
Balances at December 31, 2011	15,458,796	$ 25,738	2,451,184	$ 495	4,132,530	$ 41	(7,650)	$ (176)	$ 81,942	$ (104,836)	$(23,029)
Stock-based compensation	–	–	–	211	–	–	–	–	275	–	275
Accretion of Series AA preferred stock issuance costs	–	45	–	–	–	–	–	–	(45)	–	(45)
Accrual of Series AA preferred stock dividends	–	2,073	–	–	–	–	–	–	(2,073)	–	(2,073)
Net loss	–	–	–	–	–	–	–	–	–	(6,058)	(6,058)
Balances at December 31, 2012	15,458,796	27,856	2,451,184	706	4,132,530	41	(7,650)	(176)	80,099	(110,894)	(30,930)
Repurchase of Series X preferred stock	–	–	(558,864)	(343)	–	–	–	–	–	–	–
Stock-based compensation	–	–	–	185	–	–	–	–	10	–	10
Issuance of Series AA preferred stock and Series AA preferred stock warrants, net of issuance costs	6,540,221	8,377	–	–	–	–	–	–	–	–	–
Issuance of Series AA preferred stock upon conversion of convertible notes and accrued interest	2,677,731	4,093	–	–	–	–	–	–	–	–	–
Conversion of Series AA preferred stock into common stock	(1,471,965)	(2,253)	–	–	14,719	–	–	–	2,253	–	2,253
Accretion of Series AA preferred stock to redemption value	–	380	–	–	–	–	–	–	(380)	–	(380)
Accrual of Series AA preferred stock dividends	–	2,232	–	–	–	–	–	–	(2,232)	–	(2,232)
Net loss	–	–	–	–	–	–	–	–	–	(7,616)	(7,616)
Balances at December 31, 2013	23,204,783	40,685	1,892,320	548	4,147,249	41	(7,650)	(176)	79,750	(118,510)	(38,895)
Stock-based compensation (unaudited)	–	–	–	–	–	–	–	–	4	–	4
Accretion of Series AA preferred stock to redemption value (unaudited)	–	419	–	–	–	–	–	–	(419)	–	(419)
Accrual of Series AA preferred stock dividends (unaudited)	–	1,611	–	–	–	–	–	–	(1,611)	–	(1,611)
Net loss (unaudited)	–	–	–	–	–	–	–	–	–	(4,995)	(4,995)
Balances at June 30, 2014 (unaudited)	23,204,783	42,715	1,892,320	548	4,147,249	41	(7,650)	(176)	77,724	(123,505)	(45,916)
Conversion off redeemable convertible preferred stock into common stock (unaudited)	(23,204,783)	(42,715)	(1,893,320)	(548)	30,450,953	305	–	–	42,598	–	43,263
Reclassification of warrants to purchase preferred stock to stockholders' deficit (unaudited)	–	–	–	–	–	–	–	–	2,486	–	2,486
Pro forma balances—June 30, 2014 (unaudited)	–	$ –	–	$ –	34,598,202	$ 346	(7,650)	$ (176)	$ 123,168	$ (123,505)	$ (167)

The accompanying notes are an integral part of these consolidated financial statements.

Inotek Pharmaceuticals Corporation

Consolidated Statements of Cash Flows
(in thousands, except share and per share amounts)

	Year Ended December 31,		Six months Ended June 30,	
	2012	2013	2013	2014
			(unaudited)	
Cash flows from operating activities:				
Net loss	$(6,058)	$ (7,616)	$ (3,713)	$ (4,995)
Adjustments to reconcile net loss to cash used by operating activities:				
Depreciation	9	–	–	–
Noncash interest expense	213	492	381	106
Change in fair value of warrant liabilities	—	81	–	598
Stock-based compensation	486	(148)	(153)	4
Loss on sale of property and equipment	2	–	–	–
Changes in operating assets and liabilities:				
Prepaid expenses and other assets	43	(21)	12	26
Accounts payable	159	(158)	(45)	130
Accrued expenses and other current liabilities	(1,790)	915	880	219
Net cash used in operating activities	(6,936)	(6,455)	(2,638)	(3,912)
Cash flows from investing activities:				
Proceeds from sale of property and equipment	3	–	–	–
Net cash provided by investing activities:	3	–	–	–
Cash flows from financing activities:				
Net proceeds from issuance of notes payable and Series AA preferred stock warrants	–	6,915	6,915	–
Proceeds from issuance of convertible notes	2,500	1,000	1,000	–
Net proceeds from issuance of Series AA preferred stock and Series AA preferred stock warrant	–	9,961	8,675	–
Net cash provided by financing activities:	2,500	17,876	16,590	–
Net change in cash and cash equivalents	(4,433)	11,421	13,952	(3,912)
Cash and cash equivalents, beginning of period	5,805	1,372	1,372	12,793
Cash and cash equivalents, end of period	$ 1,372	$12,793	$15,324	$ 8,881
Supplemental disclosure of cash flow information:				
Cash paid for interest	$ –	$ 389	$ –	$ 385
Supplemental disclosure of noncash investing and financing activities:				
Accrual of Series AA preferred stock dividends	$ 2,073	$ 2,232	$ 1,126	$ 1,611
Issuance of 2,677,731 shares of Series AA preferred stock upon conversion of convertible notes and accrued interest	$ –	$ 4,093	$ 4,093	$ –
Accretion of Series AA preferred stock to redemption value	$ 45	$ 380	$ 25	$ 419
Conversion of Series AA preferred stock to common stock	$ –	$ 2,253	$ –	$ –

The accompanying notes are an integral part of these consolidated financial statements.

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

1. Organization and Operations

Inotek Pharmaceuticals Corporation (the "Company") is a clinical-stage biopharmaceutical company advancing molecules with novel mechanisms of action to address significant diseases of the eye. The Company's business strategy is to develop and progress its product candidates through human clinical trials. The Company's headquarters are located in Lexington, Massachusetts.

The Company has devoted substantially all of its efforts to research and development, including clinical trials of its product candidates. The Company has not completed the development of any product candidates. The Company has no current source of revenue to sustain present activities and does not expect to generate revenue until and unless the Company receives regulatory approval of and successfully commercializes its product candidates. The Company is subject to a number of risks and uncertainties similar to those of other life science companies developing new products, including, among others, the risks related to the necessity to obtain adequate additional financing, to successfully develop product candidates, to obtain regulatory approval of products candidates, to comply with government regulations, to successfully commercialize its potential products, to the protection of proprietary technology and to the dependence on key individuals.

Liquidity

The accompanying consolidated financial statements have been prepared on a basis that assumes the Company will continue as a going concern, which contemplates the realization of assets and the satisfaction of liabilities and commitments in the normal course of business. The Company has funded its operations to date primarily through the sale of preferred stock and issuance of convertible promissory notes and notes payable. The Company will need to expend substantial resources for research and development, including costs associated with the clinical testing of its product candidates and will need to obtain additional financing to fund its operations and to conduct trials for its product candidates. If such products were to receive regulatory approval, the Company would need to prepare for the potential commercialization of its product candidates and fund the commercial launch and continued marketing of its products. The Company expects operating expenses will substantially increase in the future related to additional clinical testing and to support an increased infrastructure to support expanded operations.

As of June 30, 2014, the Company has an accumulated deficit of $123,505. The Company has $8,881 of cash as of June 30, 2014 which is expected to fund operations through the first quarter of 2015. The future need for operating capital and research and development funding significantly exceeds this amount and as a result, the Company will require additional funding in the future and may not be able to raise such additional funds. The Company expects losses will continue as it conducts research and development activities. The Company will seek to finance future cash needs through public or private equity offerings, license agreements, debt financings, collaborations, strategic alliances, or any combination thereof. The incurrence of indebtedness would result in increased fixed payment obligations and could also result in restrictive covenants, such as limitations on our ability to incur additional debt, limitations on the Company's ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact the ability of the Company to conduct its business. If adequate funds are not available, the Company would delay, reduce or

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

eliminate research and development programs and reduce administrative expenses. The Company may seek to access the public or private capital markets whenever conditions are favorable, even if it does not have an immediate need for additional capital at that time. In addition, if the Company raises additional funds through collaborations, strategic alliances or licensing arrangements with third parties, it may have to relinquish valuable rights to its technologies, future revenue streams or product candidates or to grant licenses on terms that may not be favorable to it. If the Company is unable to raise sufficient funding, it may be unable to continue to operate. There is no assurance that the Company will be successful in obtaining sufficient financing on acceptable terms and conditions to fund continuing operations, if at all. The failure of the Company to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on the Company's business, results of operations and financial condition.

2. Significant Accounting Policies

Basis of Presentation—The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP").

Principles of Consolidation—The consolidated financial statements include the accounts of the Company and results of its wholly owned subsidiaries which ceased operations in 2010. All subsidiaries were dissolved by December 31, 2012, and results from their operations were insignificant during the year ended December 31, 2012. The Company currently has no subsidiaries.

Segment Reporting—Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment, that of developing pharmaceutical product candidates with the intention of achieving marketing approval and commercializing the approved products. All operations are located in the United States.

Unaudited Pro Forma Presentation—In August 2014, the Company's board of directors authorized the Company to submit a draft registration statement to the Securities and Exchange Commission permitting the Company to sell shares of its common stock to the public. The unaudited pro forma balance sheet as of June 30, 2014 reflects the automatic conversion of all of the shares of Preferred Stock (Note 7) and accrued dividends thereon into 30,450,953 shares of common stock.

Unaudited pro forma net loss per share is computed using the weighted average number of shares of common stock outstanding after giving effect to the conversion of all Preferred Stock during the year ended December 31, 2013 and the six months ended June 30, 2014 into shares of the Company's common stock as if such conversion had occurred at the date the Company issued such shares or the beginning of the applicable period, as appropriate.

Unaudited Interim Financial Information—The accompanying balance sheet as of June 30, 2014, statements of operations and cash flows for the six months ended June 30, 2013 and 2014, and consolidated statements of changes in redeemable convertible preferred stock and stockholders' deficit

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

for the six months ended June 30, 2014, are unaudited. The interim unaudited consolidated financial statements have been prepared on the same basis as the annual audited consolidated financial statements and, in the opinion of management, reflect all adjustments, which include normal recurring adjustments, necessary for the fair presentation of the Company's financial position as of June 30, 2014, and the results of its operations and its cash flows for the six months ended June 30, 2013 and 2014. The financial data and other information disclosed in these notes related to the six months ended June 30, 2013 and 2014 and as of June 30, 2014, are unaudited. The results for the six months ended June 30, 2014, are not indicative of results to be expected for the year ending December 31, 2014, any other interim periods or any future year or period.

Use of Estimates—The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reporting period. Actual results could differ from these estimates. Significant items subject to such estimates and assumptions include the valuation of stock options used for the calculation of stock-based compensation, fair value of warrant liabilities and determination of accruals related to research and clinical development.

Cash and Cash Equivalents—Cash and cash equivalents consists of bank deposits and money market accounts. Cash equivalents are carried at cost which approximates fair value due to their short-term nature and which the Company believes do not have a material exposure to credit risk. The Company considers all highly liquid investments with maturities of three months or less from the date of purchase to be cash equivalents.

The Company maintains its cash and cash equivalent balances in the form of money market accounts with financial institutions that management believes are creditworthy. The Company's cash and cash equivalent accounts, at times, may exceed federally insured limits. The Company has not experienced any losses in such accounts. The Company believes it is not exposed to any significant credit risk on cash and cash equivalents.

Deferred Financing Costs—Financing costs incurred in connection with the Company's notes payable and convertible promissory notes were capitalized at the inception of the notes and amortized over the term of the respective notes using the effective interest rate method. Amortization of deferred financing costs were $0 and $112 in the years ended December 31, 2012 and 2013, respectively, and $0 and $106 in the six months ended June 30, 2013 and 2014, respectively (see Note 5).

Research and Development Costs—Research and development costs are charged to expense as incurred and include, but are not limited to:

- employee-related expenses including salaries, benefits, travel and stock-based compensation expense for research and development personnel;
- expenses incurred under agreements with contract research organizations that conduct clinical and preclinical studies, contract manufacturing organizations and consultants;

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

- costs associated with preclinical and development activities; and
- costs associated with regulatory operations.

Costs for certain development activities, such as clinical studies, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, and information provided to the Company by its vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the patterns of costs incurred, and are reflected in the consolidated financial statements as accrued expenses.

Stock-Based Compensation—The Company measures the cost of employee services received in exchange for an award of equity instruments based on the fair value of the award on the grant date. That cost is recognized on a straight-line basis over the period during which the employee is required to provide service in exchange for the award. The fair value of options on the date of grant is calculated using the Black-Scholes option pricing model based on key assumptions such as stock price, expected volatility and expected term. The Company's estimates of these assumptions are primarily based on third-party valuations, historical data, peer company data and judgment regarding future trends and factors.

The Company accounts for stock options issued to non-employees in accordance with the provisions of the Financial Accounting Standards Board ("FASB") Accounting Standard Codification ("ASC") 505-50, *Equity-Based Payments to Non-employees*, which requires valuing the stock options on their grant date and remeasuring such stock options at their current fair value as they vest.

The Company has not granted any stock options since 2009. During 2010, the Company issued shares of Series X preferred stock to certain employees and consultants (Note 7).

Fair Value Measurements—The Company is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. ASC 820, *Fair Value Measurements and Disclosures* ("ASC 820"), establishes a hierarchy of inputs used when available. Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances. The fair value hierarchy applies only to the valuation inputs used in determining the reported fair value of the investments and is not a measure of the investment credit quality. The three levels of the fair value hierarchy are described below:

Level 1—Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.

Level 2—Valuations based on quoted prices for similar assets or liabilities in markets that are not active or for which all significant inputs are observable, either directly or indirectly.

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

Level 3—Valuations that require inputs that reflect the Company's own assumptions that are both significant to the fair value measurement and unobservable.

To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement. The Company's assets and liabilities measured at fair value on a recurring basis include cash equivalents and warrant liabilities (Note 9).

Income taxes—The Company uses the asset and liability method for accounting for income taxes. Under this method, deferred tax assets and liabilities are recognized for the estimated future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective income tax bases. Deferred tax assets and liabilities are measured using enacted rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. A valuation allowance is recorded if it is more likely than not that a deferred tax asset will not be realized. The Company has provided a full valuation allowance on its deferred tax assets.

The Company recognizes the financial statement benefit of a tax position only after determining that the relevant tax authority would more likely than not sustain the position following an audit. For tax positions meeting the more-likely-than-not threshold, the amount recognized in the consolidated financial statements is the largest benefit that has a greater than 50 percent likelihood of being realized upon ultimate settlement with the relevant tax authority.

The Company will recognize interest and penalties related to uncertain tax positions in income tax expense. As of and for the periods ended December 31, 2012 and 2013 and June 30, 2013 and 2014, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's consolidated statements of operations.

Net loss per share—The Company calculates net loss per share in accordance with ASC 260, *Earnings per Share*. Basic earnings (loss) per share ("EPS") is calculated by dividing the net income or loss applicable to common stockholders by the weighted average number of common shares outstanding for the period, without consideration of unissued common stock equivalents. The net loss applicable to common stockholders is determined by the reported net loss for the period and deducting dividends accrued and accretion of preferred stock. Diluted EPS is calculated by adjusting the weighted average common shares outstanding for the dilutive effect of common stock options, warrants, and convertible preferred stock and accrued but unpaid convertible preferred stock dividends. In periods where a net loss is recorded, no effect is given to potentially dilutive securities, as their effect would be anti-dilutive.

Unaudited pro forma net loss per share is computed using the weighted average number of shares of common stock outstanding after giving effect to the conversion of all convertible preferred stock and

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

accrued but unpaid convertible preferred stock dividends during the year ended December 31, 2013 and the six months ended June 30, 2014 into shares of the Company's common stock as if such conversion had occurred at the date the Company issued such shares or the beginning of the applicable period, as appropriate.

The following table sets forth the computation of basic and diluted earnings (loss) per share attributable to the Company's common stockholders:

	December 31,		June 30,	
	2012	2013	2013	2014
Numerator:				
Net loss	$ (6,058)	$ (7,616)	$ (3,713)	$ (4,995)
Accretion and dividends on convertible preferred stock	(2,118)	(2,612)	(1,151)	(2,030)
Net loss applicable to common stockholders	$ (8,176)	$ (10,228)	$ (4,864)	$ (7,025)
Denominator:				
Weighted average common shares outstanding—basic and diluted	4,124,880	4,131,863	4,124,880	4,139,599
Net loss per share applicable to common stockholders—basic and diluted	$ (1.98)	$ (2.48)	$ (1.18)	$ (1.70)

The following common stock equivalents were excluded from the calculation of diluted net loss per share for the periods indicated as including them would have an anti-dilutive effect:

	December 31, 2012	December 31, 2013	June 30, 2013	June 30, 2014
Series AA preferred stock	15,458,796	23,204,783	23,824,518	23,204,783
Series X preferred stock	2,451,184	1,892,320	1,892,320	1,892,320
Warrants for Series AA preferred stock	–	1,081,226	228,906	1,081,226
Stock options	53,542	48,137	48,137	48,137
Total	17,963,522	26,226,466	25,993,881	26,226,466

Subsequent Events—The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the financial statements to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. The Company has completed an evaluation of all subsequent events through the date the financial statements were issued.

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

3. Property and Equipment

At December 31, 2012 and 2013 and June 30, 2014, the Company's property and equipment consisted of the following:

	Estimated Useful Life	December 31, 2012	December 31, 2013	June 30, 2014
Office equipment	5 years	$ 50	$ 50	$ 50
Computer hardware and software	3 – 5 years	167	167	167
Total		217	217	217
Less accumulated depreciation		(217)	(217)	(217)
Property and equipment, net		$ –	$ –	$ –

During the year ended December 31, 2012, the Company recognized $9 of depreciation expense. During the year ended December 31, 2013, and the six month periods ended June 30, 2013 and 2014, the Company did not recognize any depreciation expense as its assets were fully depreciated.

4. Accrued Expenses

Accrued expenses at December 31, 2012 and 2013 and June 30, 2014 consisted of the following:

	December 31, 2012	December 31, 2013	June 30, 2014
Research and development	$144	$ 858	$1,206
Government payable	367	394	408
Compensation and benefits	86	213	62
Professional fees	52	110	110
Other	16	4	12
Total	$665	$1,579	$1,798

5. Debt

Notes Payable

On June 28, 2013, the Company entered into two Loan and Security Agreements (the "Loan Agreements" or "Loans") with two financial entities (the "Lenders") pursuant to which the Company issued Loans for $3,500 to each lender and received proceeds of $6,915 net of costs and fees payable to the lenders. The Loans bear interest at a rate per annum of 11.0%. The Loans mature on October 1, 2016 and require interest-only payments for the initial 12 months and thereafter require repayment of the principal balance with interest in 27 monthly installments. Also, upon full repayment or maturity of the Loans, the Lenders are due a termination payment of 3.0% of the initial principal amount of the Loans, or $210 (the "Loan Termination Payment"). In connection with the Loan Agreements, the Company granted first priority liens and the Loans are collateralized by the Company's personal property, including cash and cash equivalents. The Loan Agreements contain representations and warranties by the Company and certain indemnification provisions, non-financial covenants and default provisions. The Loan

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

Agreements also include certain provisions allowing for prepayment of the debt by the Company, exercisable at the Company's option, which require payment of additional interest to the Lenders based upon a stated rate and the balance outstanding at repayment. The Company has determined that the various embedded features do not require bifurcation from the Loan Agreements.

In connection with the Loan Agreements, the Company issued to the Lenders fully-vested warrants to purchase either, at the election of the warrant holder, (i) 228,906 shares of the Company's Series AA preferred stock at an exercise price of $1.529 per share, or (ii) $350 of stock in the next round stock, as defined in the Loan Agreements, at a price that is the lowest effective price per share that is offered in the next round. The warrants expire on the earlier of (i) ten years after the date of grant, or (ii) immediately prior to an acquisition transaction, as defined in the warrants.

The Company recorded the fair value of the warrant of approximately $222 (Note 9) as a discount to the carrying value of the Loans and as a liability. The Company will recognize any change in the value of the warrant liability each reporting period in the statement of operations. Additionally, the Company incurred fees related to the Loan Agreements and reimbursed Lenders for costs incurred by them aggregating $85 and reflected these fees as a discount to the carrying value of the Loan. The Company amortizes these loan discounts and the Loan Termination Payment, together totaling $517, to interest expense over the term of the Loan using the effective interest rate method. For the year ended December 31, 2013, interest expense related to the Loan Agreements was $501, including $112 related to accretion of the debt discount and termination payment. For the six months ended June 30, 2014, interest expense related to the Loan Agreements was $491, including $106 related to accretion of the debt discount and termination payment. At December 31, 2013 and June 30, 2014, the principal balance on the Loan Agreements was $7,000 and the unamortized debt discount balance was $195 and $89, respectively. Principal payments on the Loans are scheduled to be $1,410 in 2014, $3,063 in 2015 and $2,527 in 2016.

Convertible Promissory Notes

On July 2, 2012, the Company entered into convertible note purchase agreements (the "Convertible Note Agreements") with 11 of its principal investors pursuant to which the investors agreed to make loans to the Company in installments aggregating $3,500 in exchange for 8% convertible promissory notes (the "Convertible Notes"). The Convertible Notes' maturity date was July 2, 2013.

In July and November 2012, $1,500 and $1,000, respectively, of Convertible Notes were issued by the Company and reflected as a current liability at December 31, 2012.

The Convertible Notes plus the accrued interest thereon were convertible into shares issued in the Company's next sale of preferred stock on or before the maturity date of the Convertible Notes in an amount of at least $10,000 from one or more institutional investors. The conversion price was at a 10% discount from the issue price of such preferred stock. Based upon the terms of the Convertible Notes, and the intention to convert the notes prior to maturity, the Company deemed the Convertible Notes to be share-settled debt, and the Company accreted the Convertible Notes over their term, to the value of

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

the preferred stock into which the Convertible Notes would be converted ($3,909), recognizing accretion of this $409 discount as interest expense.

Pursuant to the terms of the Convertible Note Agreements, if a change-in control event, as defined in the Convertible Note Agreements, occurred prior to repayment or conversion of the Convertible Notes, the Convertible Noteholders would be entitled to receive in cash, an amount equal to two times the principal plus accrued interest. This feature was determined to be an embedded derivative. The Company bifurcated the derivative and accounted for it separately determining the value of the derivative to be de minimis. The Company reassessed the value of the derivative at each reporting period, concluding that the value remained de minimis.

During the years ended December 31, 2012 and 2013 and the six months ended June 30, 2013, the Company recorded $213, $381 and $381, respectively, of non-cash interest expense related to the accretion of the conversion feature and the accrual of interest on the Convertible Notes.

On June 11, 2013, pursuant to the provisions of the Convertible Note Agreements and in connection with the Company's issuance of Series AA preferred stock (see Note 7), the carrying value of the Convertible Notes of $3,909 and accrued interest of $185 were converted into 2,677,731 shares of Series AA preferred stock.

6. Income Taxes

No provision for federal or state income taxes was recorded during the years ended December 31, 2012 and December 31, 2013, as the Company incurred operating losses for each of these years.

A reconciliation between the effective tax rates and statutory rates for the years ended December 31, 2012 and 2013 is as follows:

	December 31,	
	2012	2013
Computed at statutory rate	34.00%	34.00%
State income taxes	5.46%	5.44%
Tax credits	0.00%	4.41%
Other	(1.82%)	(0.51%)
Valuation allowance	(37.64%)	(43.34%)
	–%	–%

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

The tax effect of significant temporary differences representing deferred tax assets and liabilities as of December 31, 2012 and 2013 is as follows:

	December 31,	
	2012	2013
Net operating loss ("NOL") and credit carryforwards	$ 25,255	$ 28,490
Capitalized research and development costs	11,786	11,890
Capital loss carryover	1,672	1,672
Other	221	183
Valuation allowance	(38,934)	(42,235)
	$ –	$ –

As required by ASC 740, *Income Taxes*, management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which are comprised principally of NOL carryforwards and capitalized research and development costs. As a result of the fact that the Company has incurred tax losses from inception, management has determined that it is more likely than not that the Company will not recognize the benefits of federal and state net deferred tax assets and, as a result, a full valuation allowance has been established against its net deferred tax assets as of December 31, 2012 and 2013. The Company has offset certain deferred tax liabilities with deferred tax assets that are expected to generate offsetting deductions within the same period. During the years ended December 31, 2012 and 2013, the valuation allowance changed by $2,300 and $3,301, respectively. Realization of deferred tax assets is dependent upon the generation of future taxable income.

As of December 31, 2013, the Company had federal NOL carryforwards for income tax purposes of approximately $69,300 that expire at various dates through 2033, and state NOL carryforwards of approximately $45,200 that expire at various dates through 2033, available to reduce future federal and state income taxes, if any. As of December 31, 2013, the Company had federal research and development tax credits of approximately $2,466, and state research and development tax credits of approximately $526. If substantial changes in the Company's ownership should occur, as defined in Section 382 of the Internal Revenue Code of 1986, as amended, (the "Code"), there could be annual limitations on the amount of loss carryforwards which can be realized in future periods. The Company has determined that it has experienced a prior ownership change occurring in 2006. The pre-change NOLs, although subject to an annual limitation, can be utilized in future years as well as any post change NOLs, provided that sufficient income is generated and no future ownership changes occur that may limit the Company's NOLs. The Company does not believe it has experienced an ownership change since 2006.

As of December 31, 2012 and 2013, the Company's total unrecognized tax benefits totaled $235 and $258, respectively, which if recognized would affect the effective tax rate prior to the adjustment for the Company's valuation allowance. The Company files income tax returns in the U.S. federal and Massachusetts tax jurisdictions. Tax years 2010 through 2013 remain open to examination by the tax jurisdictions to which the Company is subject to tax. Since the Company is in a loss carryforward

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

position, the Internal Revenue Service ("IRS") and state taxing authorities are permitted to audit the earlier tax years and propose adjustments up to the amount of the NOLs, generated. The Company is not currently under examination by the IRS or any other jurisdiction for any tax years.

The change in unrecognized tax benefits for each of the years ended December 31, 2012 and 2013 are as follows:

	December 31,	
	2012	2013
Balance at January 1,	$220	$235
Additions for current year tax positions	15	23
Reductions for expirations of statute of limitations or settlements	–	–
	$235	$258

The Company does not expect significant changes in its unrecognized tax benefits over the next twelve months.

7. Equity

Authorized Shares

As of December 31, 2013, the authorized stock of the Company was 32,857,171 shares of common stock, $0.01 par value per share, and 28,659,924 shares of preferred stock, $0.001 par value per share, of which 25,757,874 shares are authorized Series AA redeemable convertible preferred stock (the "Series AA preferred stock") and 2,902,050 shares are authorized as Series X redeemable convertible preferred stock (the "Series X preferred stock") (collectively, the "Preferred Stock").

Common Stock

All preferences, voting powers, relative, participating, optional, or other specific rights and privileges, limitations, or restrictions of the common stock are expressly subject to those that may be fixed with respect to any shares of preferred stock. Common stockholders are entitled to one vote per share, and to receive dividends, when and if declared by the Board. At December 31, 2012, there were 4,124,880, shares of common stock outstanding and at each of December 31, 2013 and June 30, 2014, there were 4,139,599, shares of common stock outstanding.

Preferred Stock

The Company has evaluated the tranched nature of its Preferred Stock offerings, its investor registration rights, as well as the rights, preferences and privileges of each series of Preferred Stock and has concluded that there are no freestanding derivative instruments or any embedded derivatives requiring bifurcation. Additionally, the Company assessed the conversion terms associated with its Preferred Stock and concluded that there were no beneficial conversion features.

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

Series AA Redeemable Convertible Preferred Stock

As of December 31, 2011, there were 15,458,796 shares of Series AA preferred stock issued and outstanding.

In June and July 2013, the Company issued 6,540,221 shares of Series AA preferred stock at a price per share of $1.529 for cash proceeds in the amount of $9,961, net of issuance costs of $39.

In connection with these financings, the Company issued 2,677,731 shares of Series AA preferred stock pursuant to conversion of the Convertible Notes (see Note 5).

Certain investors did not purchase their prescribed pro-rata shares, as defined in the Series AA convertible preferred stock and warrant purchase agreements and in accordance therewith 1,471,965 shares of their previously outstanding Series AA preferred stock were converted into 14,719 shares of common stock and the $2,253 carrying value of the converted Series AA preferred stock was reclassified to additional paid-in capital.

Additionally, the Company issued warrants to purchase 852,230 shares of Series AA preferred stock at a price of $0.01 per share. These warrants expire upon the earliest of (i) the tenth anniversary of issuance, or July 11, 2023, (ii) the closing of the Company's initial public offering of its securities, or (iii) the closing of a sale event, as defined in the warrant. The Company allocated $1,585 of the proceeds received, representing the grant date fair value, to the warrants issued and accounts for these warrants as liabilities. The Company will recognize any change in the fair value of the warrant liabilities each reporting period in the consolidated statements of operations (Note 9).

Due to the optional redemption feature of the Series AA preferred stock, the Company classifies the Series AA preferred stock as temporary equity in the mezzanine section of the balance sheet and is accreting the value to the redemption amount. The carrying amount of the Series AA preferred stock at December 31, 2012 was $27,856, including $4,343 of accrued but unpaid and undeclared dividends. The carrying amount of the Series AA preferred stock at December 31, 2013 was $40,685, including $6,575 of accrued but unpaid and undeclared dividends. The carrying amount of the Series AA preferred stock at June 30, 2014, was $42,715, including $8,186 of accrued but unpaid and undeclared dividends.

Rights, Preferences, and Privileges

Voting:

Series AA preferred stock votes together with all other classes and series of stock as a single class on all actions to be taken by the stockholders of the Company. Each share of Series AA preferred stock shall entitle the holder to such number of votes per share on each such action as shall equal the number of shares of common stock (including fractions of a share) into which each share of Series AA preferred stock is then convertible.

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

Dividends:

Series AA preferred stock accrues dividends quarterly at the rate of eight percent (8%) per annum, based upon the Series AA original issue price, whether or not declared, are cumulative and compounded annually. The Series AA original issue price was $1.529 per share (“Series AA Original Issue Price”).

Liquidation Preference:

Upon any liquidation, dissolution or winding up of the Company (a “Liquidation Event”), whether voluntary or involuntary, the holders of the shares of Series AA preferred stock shall be paid out of the assets of the Company available for distribution to its stockholders before any payment shall be made to the holders of Series X preferred stock or common stock, an amount per share equal to two times the Series AA Original Issue Price plus any accrued or declared but unpaid dividends (the “Series AA Initial Preference”). If upon any Liquidation Event, the assets to be distributed to the holders of Series AA preferred stock shall be insufficient to permit payment to the stockholders of the Series AA Initial Preference, then the holders of the Series AA preferred stock shall share ratably in any distribution of the remaining assets of the Company available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the shares held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full.

Upon any Liquidation Event, immediately after the holders of Series AA preferred stock have been paid in full the Series AA Initial Preference and after the holders of Series X preferred stock have been paid full the Series X preference (see Series X preferred stock below), the holders of the shares of Series AA preferred stock shall be paid out of the assets of the Company available for distribution to its stockholders before any payment shall be made to the holders of common stock, a per share amount equal to one-half times the Series AA Original Issue Price (the “Series AA Secondary Preference”). If upon any Liquidation Event, the assets to be distributed to the holders of Series AA preferred stock shall be insufficient to permit payment to such stockholders of the Series AA Secondary Preference, then the holders of the Series AA preferred stock shall share ratably in any distribution of the remaining assets of the Company available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the shares held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full.

Optional Conversion:

The holder of any share or shares of Series AA preferred stock shall have the right, at its option at any time, to convert any such shares of Series AA preferred stock (except that upon any liquidation of the Company the right of conversion shall terminate at the close of business on the business day fixed for payment of the amounts distributable on the Series AA preferred stock), each such share of Series AA preferred stock being converted into such number of fully paid and nonassessable shares of common stock as is obtained by dividing (1) the Series AA Original Issue Price plus any accrued or declared but unpaid dividends by (2) the Series AA Conversion Price in effect at the date any share or shares of Series AA preferred stock are surrendered for conversion. The “Series AA Conversion Price” is $ 1.529, and is subject to adjustment as discussed under the section “Anti Dilution” below.

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

Mandatory Conversion:

The Series AA preferred stock (including any accrued and unpaid dividends thereon) shall be automatically converted into common stock, at the then applicable conversion price (i) in the event that the holders of at least two-thirds of the outstanding Series AA preferred stock, voting as a single class, consent to such conversion, or (ii) upon the closing of a firmly underwritten public offering (a "Qualified Public Offering") of shares of common stock of the Company at a price per share of not less than $7.65 per share and a total gross offering proceeds to the Company in excess of $40,000 (before deduction of underwriters' commissions and discounts). The Qualified Public Offering shall be underwritten by an investment bank approved by a majority of the board of directors and acceptable to two-thirds of the Series AA preferred stock.

Special Mandatory Conversion:

In the event that any investor does not participate in a qualified financing by purchasing in the aggregate, in such qualified financing and within the time period specified by the Company its pro rata amount of the qualified financing (such Investor's "Pro Rata Amount"), then the applicable portion of the shares of Series AA preferred stock held by such investor immediately prior to the initial closing of the qualified financing shall automatically, and without any further action on the part of such Investor, be converted into common stock at a conversion ratio of one hundred-to-one (100:1) (such that every one hundred shares of Series AA preferred Stock are converted into one share of common stock), effective upon, subject to, and concurrently with, the consummation of the final closing. For purposes of determining the number of shares of Series AA preferred stock owned by an investor, and for determining the number of offered securities an investor has purchased in a qualified financing, all shares of Series AA preferred stock held by affiliates of such investor shall be aggregated with such investor's shares and all offered securities purchased by affiliates of such Investor shall be aggregated with the offered securities purchased by such Investor (provided that no shares or securities shall be attributed to more than one entity or person within any such group of affiliated entities or persons).

Anti-dilution:

The conversion price of the Series AA preferred stock is subject to adjustment to reduce dilution in the event that the Company issues additional equity securities at a purchase price less than the applicable conversion price. The conversion price will also be subject to proportional adjustment for events such as stock splits, stock dividends, and recapitalization.

Redemption:

Shares of Series AA preferred stock shall be redeemed by the Company out of funds lawfully available there for at a price equal to the Series AA Original Issue Price per share, plus all accrued or declared but unpaid dividends thereon (the "Redemption Price"), in three annual installments commencing not more than 60 days after receipt by the Company at any time on or after the fifth anniversary of June 9, 2010, from the holders of at least sixty-six and two-thirds percent (66 and 2/3%) of the then outstanding shares of Series AA preferred stock of written notice requesting redemption of all shares of Series AA preferred stock. The date of each such installment shall be referred to as a

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

"Redemption Date." If the Company does not have sufficient funds legally available to redeem on any Redemption Date all shares of Series AA preferred stock to be redeemed on such Redemption Date, the Company shall redeem a pro rata portion of each holder's redeemable shares of such capital stock out of funds legally available.

Certain "change in control" events, as defined in the Company's certificate of incorporation, are considered to be liquidation events upon which the holders of Series AA preferred stock have the option to require the Company redeem the shares held, at their liquidation value, as discussed above.

Series X Redeemable Convertible Preferred Stock

In June 2010, the Company sold 2,451,184 shares of Series X redeemable convertible preferred stock ("Series X preferred stock") to employees and consultants to the Company at a purchase price of $0.001 per share, subject to stock purchase and restriction agreements. Pursuant to these agreements, the shares vest upon the third anniversary of the issuance if the purchaser of the Series X preferred shares remained an employee or maintained a business relationship with the Company. The Series X preferred stockholder cannot sell, assign, transfer, pledge, encumber or dispose of all or any of the unvested shares except to the Company. The Company determined that the issuance of these restricted shares was compensatory in nature and accounted for the issuance as stock-based compensation. The excess grant date value, over the proceeds received from each purchase was determined to be compensation expense.

Simultaneous with the issuance of Series X preferred stock, the Company entered into termination and separation agreements with certain employees and consultants who purchased 392,189 shares of Series X preferred stock. The Company determined that there was no substantive future services required of these employees and consultants and recognized all of the associated compensation expense upon issuance.

The remaining 2,058,995 shares were issued to continuing employees of the Company and the Company recognized the compensation expense on a straight-line basis over the requisite service period, net of an estimated forfeiture rate. The Company recognized compensation expense of $211 and $185 related to the vesting of these shares, during the years ended December 31, 2012 and 2013, respectively.

Two of the employees that purchased Series X preferred stock were terminated by the Company in May 2013. Upon termination, the Company repurchased an aggregate of 558,864 shares of Series X preferred stock and modified the vesting terms on the remaining 558,862 shares of Series X preferred stock held by these employees. The modified vesting terms provide that the shares will vest upon the occurrence of a liquidation event, if such liquidation event occurs within two years of the date of the modifications. The Company retains the right to repurchase the invested shares at the purchase price of $0.01 per share if a liquidation event does not occur within two years of the date of the modification. In connection with this modification, during the year ended December 31, 2013, and the six months ended June 30, 2013, the Company reversed the cumulative $343 of stock-based compensation that

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

had been recorded related to these shares. The Company has estimated the fair value of the modified award at the modification date to be $559 and will recognize the compensation expense if and when a liquidation event occurs.

The following table is a rollforward of unvested Series X preferred stock shares;

Unvested—December 31, 2011	2,451,184
Vested	–
Repurchased	–
Unvested—December 31, 2012	2,451,184
Vested	1,333,458
Repurchased	558,864
Unvested—December 31, 2013	558,862
Vested	–
Repurchased	–
Unvested—June 30, 2014	558,862

Due to the redemption feature of the Series X preferred stock, discussed further below, the Company classifies the Series X preferred stock as temporary equity in the mezzanine section of the balance sheet.

Rights, Preferences, and Privileges

Voting Rights:

The Series X preferred stock does not have any voting rights, except as related to the election of certain directors. When the Series X preferred stock has voting rights, each share of Series X preferred stock entitles the holder to such number of votes per share on each such action as shall equal the number of shares of common stock into which each share of Series X preferred stock is then convertible.

Liquidation Preference:

Upon any liquidation event, such as a liquidation, dissolution or winding up of the Company, immediately after the holders of Series AA preferred stock have been paid in full, the Series AA preferred stock initial preference as described above and before any payment is made to the holders of common stock, the holders of the shares of Series X preferred stock shall be paid out of assets of the Company available for distribution to its stockholders a per share amount determined by taking the product of (1) the percentage calculated as (i) the total number of issued and outstanding shares of common stock owned by the holders of Series X preferred stock determined on an as converted fully-diluted basis divided by (ii) the total number of issued and outstanding shares of common stock of the Company on an as converted fully diluted basis, and (2) the remaining assets of the Company available for distribution to its stockholders, and dividing such product by the number of issued and outstanding shares of Series X preferred stock (the “Series X Preference”).

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

Certain change in control events, as defined in the Company's certificate of incorporation, are considered to be liquidation events upon which the holders of Series X preferred stock have the option to require the Company redeem the shares held, at their liquidation value, as discussed above.

Right to Convert:

The holder of any share of Series X preferred stock shall have the right, at any time to convert any such share (except that upon any liquidation of the Company the right of conversion shall terminate at the close of business on the business day fixed for payment of the amounts distributable on the Series X preferred stock), into fully paid and nonassessable shares of common stock based on the Series X Conversion Ratio. The Series X Conversion Ratio shall initially be 1:1, subject to adjustment as discussed under the section "Anti-Dilution" below.

Mandatory Conversion:

The Series X preferred stock shall be automatically converted into common stock, at the then applicable conversion price (i) in the event that the holders of at least two-thirds of the outstanding Series AA preferred stock, voting as a single class, consent to such conversion, or (ii) upon the closing of a Qualified Public Offering.

Anti-Dilution:

The conversion price of the Series X preferred stock is subject to adjustment to reduce dilution in the event that the Company issues additional equity securities at a price less than the applicable conversion price. The conversion price will also be subject to proportional adjustment for events such as stock splits, stock dividends, and recapitalization.

Treasury Stock

Treasury stock of $176 at December 31, 2012 and 2013 and June 30, 2014 reflects 7,650 shares on common stock repurchased by the Company and recorded at cost.

2004 Stock Option and Incentive Plan

In July 2004, the Company's board of directors adopted the 2004 Stock Option and Incentive Plan (the "Plan") for the issuance of incentive stock options, restricted stock, and other equity awards, all for common stock, as determined by the board of directors to employees, officers, directors, consultants, and advisors of the Company and its subsidiaries. There are 82,989 shares issuable under the Plan. Only stock options were granted under the Plan. The 2004 Plan expired in February 2014 but remains effective for all outstanding options.

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

The following table summarizes the option activity for the years ended December 31, 2012 and 2013 and six months ended June 30, 2014 under the Plan:

	Year Ended December 31,				Six months ended June 30,	
	2012	Weighted-Average Exercise Price Per Share	2013	Weighted-Average Exercise Price Per Share	2014	Weighted-Average Exercise Price Per Share
Outstanding at beginning of the period	53,542	$ 10.00	53,542	$ 10.00	48,137	$ 10.00
Granted during the period	–	–	–	–	–	–
Exercised during the period	–	–	–	–	–	–
Expired during the period	–	–	(5,405)	10.00	–	–
Outstanding at end of the period	53,542	$ 10.00	48,137	$ 10.00	48,137	$ 10.00
Exercisable at end of period	49,835	$ 10.00	48,137	$ 10.00	48,137	$ 10.00
Weighted-average years remaining on contractual life	5.18		4.17		3.67	
Unrecognized compensation cost related to non-vested stock options	$ 1		$ –		$ –	

No stock options were granted or exercised from January 1, 2012 through June 30, 2014.

The Company has historically granted common stock options pursuant to the 2004 Plan at an exercise price that is not less than the fair market value of the Company's stock as determined by the board of directors, with input from management. The board of directors has historically determined the estimated fair value of the Company's common stock on the date of grant based on a number of objective and subjective factors, including external market conditions, rights and preferences of securities senior to the common stock at the time of each grant, the likelihood of achieving a liquidity event such as an initial public offering or the sale of the Company, and third party valuations.

The Company recognizes compensation expense based on the estimated grant date fair value method using the Black-Scholes valuation model. The Company reduces compensation expense for expected forfeitures, as estimated by management.

As the Company's stock is not traded publicly, the computation of expected volatility is based on the historical volatilities of peer companies. The peer companies include organizations that are in the same industry, with similar size and stage of growth. The Company estimates that the expected life of the options granted using the simplified method allowable under Staff Accounting Bulletin No. 107, *Share Based Payments*. The expected life is applied to the stock option grant group as a whole, as the Company does not expect substantially different exercise or post vesting termination behavior among its employee population. The interest rate is based on the 5-year U.S. treasury bills on the grant date of the option.

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

The Company recorded a total of $266 and $1 in the years ended December 31, 2012 and 2013, respectively, as stock-based compensation expense relating to outstanding stock options granted pursuant to the 2004 Plan. At December 31, 2012 and 2013, there was $1 and $0 of unrecognized stock-based compensation expense relating to stock options, respectively.

Restricted Common Stock

In 2011, the Company issued 98,530 restricted common shares pursuant to a stock purchase and restriction agreement for a price of $0.01 per share. The Company received $1 from the grantee. These shares vest 25% on each of the first four anniversaries of the date of grant. The following table is a rollforward of unvested restricted common shares:

Unvested shares—December 31, 2011	98,530
Shares vested	(24,632)
Unvested shares—December 31, 2012	73,898
Shares vested	(24,633)
Unvested shares—December 31, 2013	49,265
Shares vested	(24,632)
Unvested shares—June 30, 2014	24,633

The Company recorded the excess grant date fair value, over the proceeds received as compensation expense. The Company recorded $9 of stock-based compensation expense related to this award in the years ended December 31, 2012 and 2013, and $4 in each of the six months ended June 30, 2013 and 2014. At December 31, 2012 and 2013, there was $16 and $7, respectively, unrecognized compensation expense related to this grant. At June 30, 2013 and 2014, there was $12 and $3, respectively, unrecognized compensation expense related to this grant.

8. Commitments and Contingencies

Operating leases

The Company leases office space in Lexington, Massachusetts under a lease agreement expiring in March 2015. Rent expense for the years ended December 31, 2012 and 2013, was $97 and $47, respectively, and $26 and $27 for the six months ended June 30, 2013 and 2014, respectively. Future minimum rental payments under the terms of this lease are $54 and $13 for the years ended December 31, 2014 and 2015, respectively.

Indemnification Arrangements

As permitted under Delaware law, the Company's bylaws provide that the Company will indemnify any director, officer, employee or agent of the Company or anyone serving in these capacities. The maximum potential amount of future payments the Company could be required to pay is unlimited. The Company has insurance that reduces its monetary exposure and would enable it to recover a portion of

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

any future amounts paid. As a result, the Company believes that the estimated fair value of these indemnification commitments is minimal.

Throughout the normal course of business, the Company has agreements with vendors that provide goods and services required by the Company to run its business. In some instances, vendor agreements include language that requires the Company to indemnify the vendor from certain damages caused by the Company's use of the vendor's goods and/or services. The Company has insurance that would allow it to recover a portion of any future amounts that could arise from these indemnifications. As a result, the Company believes that the estimated fair value of these indemnification commitments is minimal.

9. Fair Value of Financial Measurements

Items measured at fair value on a recurring basis include cash equivalents and warrant liabilities.

The following table sets forth the Company's financial instruments that were measured at fair value on a recurring basis by level within the fair value hierarchy:

	Fair Value Measurements at December 31, 2012			
	Total	Level 1	Level 2	Level 3
Assets				
Money market mutual fund	$ 505	$ –	$ 505	$ –

	Fair Value Measurements at December 31, 2013			
	Total	Level 1	Level 2	Level 3
Assets				
Money market mutual fund	$5,009	$ –	$5,009	$ –
Liabilities				
Convertible preferred stock warrant liability	$1,888	$ –	$ –	$1,888

	Fair Value Measurements at June 30, 2014			
	Total	Level 1	Level 2	Level 3
Liabilities				
Convertible preferred stock warrant liability	$2,486	$ –	$ –	$2,486

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

The fair value of the Company's money market mutual funds is based on quoted prices on an active exchange.

As previously discussed (Notes 5 and 7), the Company has issued warrants to purchase Series AA preferred stock in connection with the 2013 Series AA preferred stock issuance and the Loan Agreements. The Series AA warrant liabilities were recorded at their fair value on the date of issuance and are remeasured on each subsequent balance sheet date, with fair value changes recognized as income (decrease in fair value) or expense (increase in fair value) in other income (expense) in the statements of operations.

As of December 31, 2013 and as of June 30, 2014, the Company used a hybrid valuation model in which a Monte Carlo simulation was used to calculate the fair value of the Company's equity securities under three scenarios including: i) an initial public offering scenario, ii) a merger or acquisition scenario or iii) a stay private scenario. The Company then probability-weighted each equity value derived from the Monte Carlo simulation based upon the Company's estimate of the likelihood of the exit scenario occurring.

The assumptions used in calculating the estimated fair value of the warrants represent the Company's best estimates and include probabilities of settlement scenarios, enterprise value, time to liquidity, risk-free interest rates, discount for lack of marketability and volatility. The estimates are based, in part, on subjective assumptions and could differ materially in the future. Generally, increases or decreases in the fair value of the underlying convertible preferred stock would result in a directionally similar impact in the fair value measurement of the warrant liability.

The following table details the assumptions used in the Monte Carlo simulation models used to estimate the fair value of the Series AA preferred stock warrants upon issuance and at each reporting period:

	June 30, 2013	December 31, 2013	June 30, 2014
Volatility	75% – 80%	60%	65%
Expected term (years)	1.50 – 1.75	1.00 – 1.25	0.50 – 0.75
Expected dividend yield	0.0%	0.0%	0.0%
Risk-free rate	0.26% – 0.31%	0.13% – 0.19%	0.06% – 0.09%

In addition to the assumptions above, the Company's estimated fair value of the Series AA preferred stock warrant liabilities is calculated using other key assumptions including the probability of an exit event, the enterprise value as determined on an income approach, and a discount for lack of marketability. Management, with the assistance of an independent valuation firm, made these subjective determinations based on available current information; however, as such information changes, so might management's determinations and such changes could have a material impact of future operating results.

Inotek Pharmaceuticals Corporation

Notes to Consolidated Financial Statements
(Information as of June 30, 2014 and for the six months ended June 30, 2013 and 2014 is unaudited)
(in thousands, except share and per share data)

During the periods presented, the Company has not changed the manner in which it values liabilities that are measured at fair value using Level 3 inputs. The Company recognizes transfers between levels of the fair value hierarchy as of the end of the reporting period. There were no transfers within the hierarchy during the years ended December 31, 2012 or 2013 and during the six months ended June 30, 2014.

The following table reflects the change in the Company's Level 3 warrant liabilities from December 31, 2012 through June 30, 3014:

	Warrant Liabilities
Balance at December 31, 2012	$ –
Issuance of warrants	222
Change in value	–
Balance at June 30, 2013	222
Issuance of warrants	1,585
Change in value	81
Balance at December 31, 2013	1,888
Change in value	598
Balance at June 30, 2014	$ 2,486

10. Retirement Plan

The Company sponsors a 401(k) savings plan (the "Savings Plan") for all eligible U.S. employees. The Company reserves the right to modify, amend, or terminate the Savings Plan. Employees may contribute up to the maximum allowed by the IRS, while the Company contributes to the plan at the discretion of the board of directors. The Company's contributions to the plan for the years ended December 31, 2012 and 2013, amounted to $28 and $23, respectively, and $10 for the six months ended June 30, 2014.

11. Subsequent events

During July and August 2014, warrants exercisable for 508,929 shares of Series AA preferred stock at $0.01 per share were exercised, resulting in proceeds to the Company of $6.

Shares

Common Stock

PROSPECTUS

Cowen and Company **Piper Jaffray**

, 2014

Through and including , 2014 (the 25th day after the date of this prospectus), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.

PART II

Information Not Required in Prospectus

Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth the fees and expenses, other than underwriting discounts and commissions, payable in connection with the registration of the common stock hereunder. All amounts are estimates except the SEC registration fee.

SEC registration fee	$ *
FINRA filing fee	*
NASDAQ listing fee	*
Blue Sky fees and expenses	*
Printing and engraving expenses	*
Legal fees and expenses	*
Accounting fees and expenses	*
Transfer agent and registrar fees and expenses	*
Miscellaneous	*
Total	$ *

* To be provided by amendment.

Item 14. Indemnification of Directors and Officers.

Section 145 of the Delaware General Corporation Law, or the DGCL, authorizes a corporation to indemnify its directors and officers against liabilities arising out of actions, suits and proceedings to which they are made or threatened to be made a party by reason of the fact that they have served or are currently serving as a director or officer to a corporation. The indemnity may cover expenses (including attorneys' fees) judgments, fines and amounts paid in settlement actually and reasonably incurred by the director or officer in connection with any such action, suit or proceeding. Section 145 permits corporations to pay expenses (including attorneys' fees) incurred by directors and officers in advance of the final disposition of such action, suit or proceeding. In addition, Section 145 provides that a corporation has the power to purchase and maintain insurance on behalf of its directors and officers against any liability asserted against them and incurred by them in their capacity as a director or officer, or arising out of their status as such, whether or not the corporation would have the power to indemnify the director or officer against such liability under Section 145.

We have adopted provisions in our certificate of incorporation and bylaws to be in effect upon the closing of this offering that limit or eliminate the personal liability of our directors to the fullest extent permitted by the DGCL, as it now exists or may in the future be amended. Consequently, a director will not be personally liable to us or our stockholders for monetary damages or breach of fiduciary duty as a director, except for liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- any unlawful payments related to dividends or unlawful stock purchases, redemptions or other distributions; or
- any transaction from which the director derived an improper personal benefit.

These limitations of liability do not alter director liability under the federal securities laws and do not affect the availability of equitable remedies such as an injunction or rescission.

In addition, our bylaws provide that:

- we will indemnify our directors, officers and, in the discretion of our board of directors, certain employees to the fullest extent permitted by the DGCL, as it now exists or may in the future be amended; and
- we will advance reasonable expenses, including attorneys' fees, to our directors and, in the discretion of our board of directors, to our officers and certain employees, in connection with legal proceedings relating to their service for or on behalf of us, subject to limited exceptions.

We have entered into indemnification agreements with each of our directors and intend to enter into such agreements with certain of our executive officers. These agreements provide that we will indemnify each of our directors, certain of our executive officers and, at times, their affiliates to the fullest extent permitted by Delaware law. We will advance expenses, including attorneys' fees (but excluding judgments, fines and settlement amounts), to each indemnified director, executive officer or affiliate in connection with any proceeding in which indemnification is available and we will indemnify our directors and officers for any action or proceeding arising out of that person's services as a director or officer brought on behalf of us and/or in furtherance of our rights. Additionally, each of our directors may have certain rights to indemnification, advancement of expenses and/or insurance provided by their affiliates, which indemnification relates to and might apply to the same proceedings arising out of such director's services as a director referenced herein. Nonetheless, we have agreed in the indemnification agreements that our obligations to those same directors are primary and any obligation of the affiliates of those directors to advance expenses or to provide indemnification for the expenses or liabilities incurred by those directors are secondary.

We also maintain general liability insurance which covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers, including liabilities under the Securities Act.

The underwriting agreement filed as Exhibit 1.1 to this registration statement provides for indemnification of us and our directors and officers by the underwriters against certain liabilities under the Securities Act and the Exchange Act.

Item 15. Recent Sales of Unregistered Securities.

The following list sets forth information as to all securities we have sold since January 1, 2011, which were not registered under the Securities Act.

(a) Issuances of Capital Stock and Warrants to Purchase Capital Stock.

1. In June 2013, we issued a Warrant to Purchase Shares of Series Preferred Stock to each of Drawbridge Special Opportunities Fund LP and Horizon Technology Finance Corporation, each exercisable for up to 114,453 shares of our Series AA preferred stock (228,906 shares in the aggregate) at $1.529 per share, as partial consideration for their provision of a credit facility to us.

2. In June 2013, we issued an aggregate of 8,365,722 shares of our Series AA preferred stock to 11 investors for aggregate consideration of approximately $8.7 million in cash and the conversion of approximately $3.7 million in convertible promissory notes. In July 2013, we issued an aggregate of 852,230 shares of our Series AA preferred stock to eight investors for aggregate consideration of $1.3 million and warrants to purchase 852,230 shares of our Series AA preferred stock at an exercise price of $0.01 per share to the same eight investors, which warrants will terminate upon the closing of this offering.

3. In May 2011, we issued an aggregate of 2,329,464 shares of our Series AA preferred stock to 11 investors for aggregate consideration of approximately $3.6 million. In June, 2011, we issued an aggregate of 3,651,425 shares of our Series AA preferred stock to 11 investors for aggregate consideration of approximately $5.5 million.

We deemed the offers, sales and issuances of the securities described in the paragraphs above to be exempt from registration under the Securities Act, in reliance on Section 4(2) of the Securities Act, including Regulation D and Rule 506 promulgated thereunder, regarding transactions by an issuer not involving a public offering. All purchasers of securities in transactions exempt from registration pursuant to Regulation D represented to us that they were accredited investors and were acquiring the shares for investment purposes only and not with a view to, or for sale in connection with, any distribution thereof and that they could bear the risks of the investment and could hold the securities for an indefinite period of time. The purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration statement or an available exemption from such registration.

(b) Grants of Stock Options.

Since January 1, 2011, we have granted stock options to purchase an aggregate of 3,652,556 shares of our common stock, at an exercise price of $1.07 per share, to employees and directors pursuant to our 2014 Stock Option and Incentive Plan. The issuances of these securities were exempt either pursuant to Rule 701 promulgated under the Securities Act, as a transaction pursuant to a compensatory benefit plan, or pursuant to Section 4(2) of the Securities Act, as a transaction by an issuer not involving a public offering. All recipients either received adequate information about us or had access, through employment or other relationships, to such information.

All certificates representing the securities issued in the transactions described in this Item 15 included appropriate legends setting forth that the securities had not been offered or sold pursuant to a registration statement and describing the applicable restrictions on transfer of the securities. There were no underwriters employed in connection with any of the transactions set forth in this Item 15.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits:

The exhibits to the registration statement are listed in the Exhibit Index to this registration statement and are incorporated herein by reference.

(b) Financial Statements Schedules:

Schedules have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes thereto.

Item 17. Undertakings.

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended, or the Act, may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is therefore unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

The Registrant hereby undertakes that:

(a) The Registrant will provide to the underwriter at the closing as specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriter to permit prompt delivery to each purchaser.

(b) For purposes of determining any liability under the Securities Act of 1933, as amended, the information omitted from a form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in the form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act of 1933, as amended, shall be deemed to be part of this registration statement as of the time it was declared effective.

(c) For the purpose of determining any liability under the Securities Act of 1933, as amended, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant has duly caused this Registration Statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Lexington, Commonwealth of Massachusetts, on , 2014.

INOTEK PHARMACEUTICALS CORPORATION

By: _____

Name: David P. Southwell
Title: President, Chief Executive Officer and Director

POWER OF ATTORNEY AND SIGNATURES

KNOW ALL BY THESE PRESENT, that each individual whose signature appears below hereby constitutes and appoints each of David P. Southwell, Rudolf Baumgartner and William McVicar as such person's true and lawful attorney-in-fact and agent with full power of substitution and resubstitution, for such person in such person's name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement (or any Registration Statement for the same offering that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933), and to file the same, with all exhibits thereto, and all documents in connection therewith, with the Securities and Exchange Commission granting unto each said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as such person might or could do in person, hereby ratifying and confirming all that any said attorney-in-fact and agent, or any substitute or substitutes of any of them, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement and Power of Attorney has been signed by the following person in the capacities and on the date indicated.

Signature	Title	Date
_____ David P. Southwell	President, Chief Executive Officer and Director (Principal Executive Officer)	, 2014
_____ Dale Ritter	Vice President—Finance (Principal Financial and Accounting Officer)	, 2014
_____ A.N. "Jerry" Karabelas, Ph.D.	Director	, 2014
_____ Ittai Harel	Director	, 2014
_____ Paul G Howes	Director	, 2014

Signature	Title	Date
Devang V. Kantesaria, M.D.	Director	, 2014
Isai Peimer	Director	, 2014
Martin Vogelbaum	Director	, 2014

EXHIBIT INDEX

Exhibit No.	Exhibit Index
1.1*	Form of Underwriting Agreement
3.1*	Fifth Amended and Restated Certificate of Incorporation of the Registrant, as amended and currently in effect
3.2*	Sixth Amended and Restated Certificate of Incorporation of the Registrant (to be effective upon the consummation of this offering)
3.3.1**	By-Laws
3.3.2**	Amendment No. 1 to By-Laws
3.3.3**	Amendment No. 2 to By-Laws
3.3.4**	Amendment No. 3 to By-Laws
3.4*	Form of Amended and Restated Bylaws of the Registrant (to be effective upon the consummation of this offering)
4.1*	Form of Common Stock certificate of the Registrant
4.2**	Third Amended and Restated Investor Rights Agreement, dated as of June 9, 2010, by and among the Registrant and each of the parties listed on Schedule A thereto
4.3.1**	Third Amended and Restated Stockholders Agreement, dated as of June 9, 2010, by and among the Registrant and each of the parties listed on Schedule I thereto, as amended and currently in effect
4.3.2**	Amendment No. 1 to the Third Amended and Restated Stockholders Agreement, dated as of June 11, 2010, by and among the Registrant and each of the parties listed on the signature pages thereto
5.1*	Opinion of Goodwin Procter LLP
10.1†**	2004 Stock Option and Incentive Plan
10.2†*	2014 Stock Option and Incentive Plan and forms of agreements thereunder
10.3†**	Letter Agreement, dated as of July 28, 2014, by and between the Registrant and David P. Southwell
10.4†**	Letter Agreement, dated as of May 2, 2007, by and between the Registrant and Dr. Rudolf A. Baumgartner, M.D., as amended and currently in effect
10.5†**	Letter Agreement, dated as of August 23, 2007, by and between the Registrant and Dr. William K. McVicar, M.D., as amended and currently in effect
10.6†*	Letter Agreement, dated as of August 28, 2014, by and between the Registrant and Dale Ritter
10.7**	Venture Loan and Security Agreement, dated as of June 28, 2013, by and among the Registrant, Horizon Technology Finance Corporation and Fortress Credit Co LLC
10.8†*	Form of Indemnification Agreement, to be entered into between the Registrant and its directors and officers
10.9**	Lease, dated as of May 11, 2012, by and between the Registrant and Farley White Kilnbrook Three, LLC, as amended and currently in effect
23.1*	Consent of McGladrey LLP
23.2*	Consent of Goodwin Procter LLP (included in Exhibit 5.1)
24.1*	Power of Attorney (included in signature page)

* To be included by amendment.
** Previously filed.
† Indicates a management contract or any compensatory plan, contract or arrangement.

GOODWIN | PROCTER

Goodwin Procter LLP
Counsellors at Law
Exchange Place
Boston, MA 02109
T: 617.570.1000
F: 617.523.1231

September 29, 2014

VIA EDGAR AND FEDERAL EXPRESS

Division of Corporation Finance
United States Securities and Exchange Commission
100 F Street, NE
Washington, D.C. 20549
Attention: Jeffrey P. Riedler

Re: Inotek Pharmaceuticals Corporation
Confidential Draft Registration Statement on Form S-1
Submitted August 29, 2014
CIK No. 0001281895

Ladies and Gentlemen:

This letter is confidentially submitted on behalf of Inotek Pharmaceuticals Corporation (the "***Company***") in response to the September 25, 2014 comment letter (the "***Comment Letter***") of the staff (the "***Staff***") of the Securities and Exchange Commission (the "***Commission***") regarding the Company's confidential submission of the Draft Registration Statement on Form S-1 which was submitted to the Commission confidentially on August 29, 2014 (the "***Draft Registration Statement***").

Concurrently with this letter, the Company is also confidentially submitting to the Commission Confidential Draft No. 2 of Registration Statement on Form S-1 (the "***Registration Statement***"), which includes changes to reflect responses to the Staff's comments.

For reference purposes, the text of the Comment Letter has been reproduced herein with responses below each numbered comment. For your convenience, we have italicized the reproduced Staff comments from the Comment Letter. Unless otherwise indicated, page references in the descriptions of the Staff's comments refer to the Draft Registration Statement, and page references in the responses refer to the Registration Statement. All capitalized terms used and not otherwise defined herein shall have the meanings set forth in the Registration Statement.

The responses provided herein are based upon information provided to Goodwin Procter LLP by the Company. In addition to submitting this letter via EDGAR, we are sending via

Federal Express two (2) copies of each of this letter and the Registration Statement (marked to show changes from the Draft Registration Statement).

General

1. *Please submit all outstanding exhibits as soon as practicable. We may have further comments upon examination of these exhibits.*

Response: The Company acknowledges the Staff's comment and respectfully advises the Staff that certain of the exhibits not filed with the Draft Registration Statement are being filed with the Registration Statement. The Company will provide the remaining exhibits as soon as practicable.

2. *Please confirm the graphics included in your registration statement are the only graphics you will use in your prospectus. If those are not the only graphics, please provide any additional graphics prior to their use for our review.*

Response: The Company acknowledges the Staff's comment and confirms that the graphics included in the Registration Statement are the only graphics the Company currently intends to use in its prospectus. If the Company decides to use any additional graphics in its prospectus, it will provide any such graphics to the Staff prior to their use for the Staff's review.

3. *Please supplementally provide us with copies of all written communications, as defined in Rule 405 under the Securities Act, that you, or anyone authorized to do so on your behalf, present to potential investors in reliance on Section 5(d) of the Securities Act, whether or not they retain copies of the communications. Similarly, please supplementally provide us with any research reports about you that are published or distributed in reliance upon Section 2(a)(3) of the Securities Act of 1933 added by Section 105(a) of the Jumpstart Our Business Startups Act by any broker or dealer that is participating or will participate in your offering.*

Response: The Company respectfully advises the Staff that it is supplementally providing the Staff with a copy of an investor presentation that was distributed during certain "testing-the-waters" meetings, and will supplementally provide copies of any written communications that the Company, or anyone authorized to do so on the Company's behalf, uses in reliance on Section 5(d) of the Securities Act.

In addition, the Company respectfully advises the Staff that no broker or dealer that is participating in this offering has published or distributed research reports about the Company in reliance on Section 2(a)(3) of the Securities Act added by Section 105(a) of the Jumpstart Our Business Startups Act. The Company undertakes to provide the Staff with copies of such reports in the event that they are published or distributed in the future.

Risk Factors

If product liability lawsuits are successfully brought against us…," page 43

4. *Please quantify the amount of your product liability insurance in this risk factor.*

Response: In response to the Staff's comment, the Company has revised the disclosure on page 43 of the Registration Statement to quantify the amount of the Company's product liability insurance.

Industry and Market Data

Industry and Market Data, page 45

5. *We note your statement that your internal research has not been verified by any independent sources. It is not appropriate to directly or indirectly disclaim liability for information in your registration statement. Accordingly, please revise your disclosure to remove any statement indicating that you have no[t] independently verified information presented in the prospectus.*

Response: In response to the Staff's comment, the Company has revised the disclosure on pages 25 and 55 of the Registration Statement to remove any statement indicating that the Company has not independently verified information presented in the prospectus.

Use of Proceeds

Use of Proceeds, page 55

6. *Please clarify in the first and second bullet whether you expect the application of funds from the offering to enable you to complete the trials in question, including the two separate planned Phase 3 trials for trabodenoson monotherapy and the Phase 2 trial for your FDC product. Otherwise, please disclose what the application of these proceeds will allow you to accomplish as to each partially funded trial.*

Response: The Company acknowledges the Staff's comment and respectfully advises the Staff that the Company is unable to estimate with certainty which clinical stage it will achieve for its product candidates with the proceeds it raises from this offering. The Company respectfully advises the Staff that it has alerted investors to the need to raise additional capital to advance the clinical development, obtain marketing authorization and ultimately commercialize its product candidates. See "Risk Factors – We will need to obtain additional financing to fund our operations…" and "Management's Discussion and Analysis of Financial Condition and Results of Operations–Liquidity and Capital Resources–Operating Capital Requirements"

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

Research and Development Expenses, page 64

7. *Please revise your disclosure for the research and development expenses by type of activity to break out expenses for trabodenoson by trabodenoson monotherapy and*

trabodenoson with latanoprost. In addition, please provide inception to date research and development expenses for each key project.

Response: In response to the Staff's comment, the Company has added disclosure of the external development costs related to *trabodenoson* from inception to date. Moreover, the Company has revised the disclosure on page 66 of the Registration Statement to indicate that the Company does not track research and development expenses for *trabodenoson* by product candidate. The Company respectfully advises the staff that research and development expenses associated with the *trabodenoson* monotherapy product candidate also benefit the *trabodenoson* with *latanoprost* product candidate; as such, the Company is unable to precisely break out research and development expenses for *trabodenoson* by product candidate and, therefore, does not track such expenses in that manner.

Contractual Obligations and Commitments, page 71

8. *Please revise your disclosure to include the interest related to the notes payable in the contractual obligations and commitments table.*

Response: In response to the Staff's comment, the Company has revised the disclosure on page 72 of the Registration Statement to include the interest related to the notes payable in the contractual obligations and commitments table.

Business

Product Pipeline, page 87

9. *The graph on this page indicates that trabodenoson plus latanoprost is currently in Phase 2, however, your disclosure elsewhere suggests you did not conduct Phase 1 for this specific treatment. Please tell us why Phase 1 trials were not conducted. If you were able to rely on safety and tolerability data from your completed Phase 1 trial of trabodenoson as a monotherapy in order to advance trabodenoson plus latanoprost directly into Phase 2 without the need for separate Phase 1 trials, please add clarifying disclosure to that effect.*

Response: In response to the Staff's comment, the Company respectfully advises the Staff that the Company did not conduct Phase 1 trials for the trabodenoson plus latanoprost fixed-dose combination treatment because the Company was able to rely on the safety and tolerability data generated in both of its completed Phase 1 trials for trabodenoson as a monotherapy. The Company has revised the disclosure on page 97 of the Registration Statement to clarify the reason why the Company did not conduct Phase 1 trials for the trabodenoson plus latanoprost fixed-dose combination treatment.

Trabodenoson, page 95

10. *We note your disclosure at page 97 with respect to the FDA requirements for long-term dosing data and a long-term safety studies for both trabodeonson monotherapy and the FDC of trabodenoson and latanoprost. In your response, please explain to us in greater*

detail why you expect the FDA will require long-term safety trials for both of your primary product candidates.

Response: In response to the Staff's comment, the Company respectfully advises the Staff that FDA exercises its legal authority to approve new drugs under the Federal Food, Drug, and Cosmetic Act (the FD&C Act), 21 U.S.C. § 355. The FD&C Act's implementing regulations at 21 C.F.R. Parts 312 and 314 describe the requirements for clinical investigations and clinical evidence of safety and effectiveness as part of an application for new drug approval (NDA). FDA also periodically issues non-binding guidance documents that describe the Agency's most recent thinking on how industry may best address issues related, in this instance, to drug approval. For example, on March 1, 1995, FDA published a Federal Register Notice entitled, "Guideline for Industry: For Drugs Intended for Long term Treatment of Non-Life-Threatening Conditions." ("Guideline"), *See*, 60 FR 11270.

The Guideline was developed in conjunction with the International Conference on Harmonization (ICH) and "… presents an accepted set of principles for the safety evaluation of drugs intended for the long-term treatment of non-life threatening diseases." It describes the extent and type of long-term safety study data that FDA will consider when reviewing therapies for chronic diseases requiring life-long treatment, such as glaucoma. Similarly, the Guideline is relevant whenever a sponsor seeks approval for its prescription drug as monotherapy and fixed-dose combination therapy. Importantly, FDA described its policy to allow fixed-dose combination drugs at 21 C.F.R. § 300.50. The regulation provides, among other things, that two or more drugs may be combined if the fixed-dose combination drug is safe and effective.

Fixed-Dose Combination of Trabodenoson and Latanoprost, page 96

11. *We note that you have an IND on file for trabodenoson on which you plan to rely for Phase 2 trials for trabodenoson in conjunction with latanoprost. In your response, please tell us the date the IND was filed and for what indication.*

Response: In response to the Staff's comment, the Company respectfully advises the Staff that the IND for *trabodenoson* to which the Staff refers was filed on January 31, 2008 (IND# 100926 SN000) for the reduction of elevated intraocular pressure in patients with ocular hypertension or primary open-angle glaucoma.

* * * *

We and the Company appreciate the Staff's attention to the review of the Registration Statement. Please do not hesitate to contact me at: (212) 813-8853 if you have any questions regarding this letter or the Registration Statement.

Sincerely,

Edwin M. O'Connor

Goodwin Procter LLP

cc: David P. Southwell, President and Chief Executive Officer, *Inotek Pharmaceuticals Corporation*
Mitchell S. Bloom, *Goodwin Procter LLP*