Filed Pursuant to Rule 424(b)(2)
Registration No. 333-206027

PROSPECTUS

5,400,000 Shares

Common Stock

We are selling 5,400,000 shares of our common stock.

Our common stock is listed on The NASDAQ Global Market under the symbol "ITEK." The closing price of our common stock on The NASDAQ Global Market on August 12, 2015, was $13.50 per share.

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012, and, as such, we have elected to take advantage of certain reduced reporting requirements for this prospectus and may elect to comply with certain reduced public company reporting requirements for future filings.

	Per Share	*Total*
Public offering price	$ 12.75	$68,850,000
Underwriting discounts and commissions(1)	$ 0.765	$ 4,131,000
Proceeds to Inotek Pharmaceuticals Corporation before expenses	$ 11.985	$64,719,000

(1) See "Underwriting" beginning on page 130 for additional information regarding underwriting compensation.

We have granted the underwriters an option to purchase up to 810,000 additional shares of our common stock at the offering price less the underwriting discount. The underwriters can exercise this right at any time within 30 days after the date of this prospectus.

Investing in our common stock involves a high degree of risk. See "Risk Factors" beginning on page 12.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares on or about August 18, 2015.

Cowen and Company **Piper Jaffray** **Nomura**

Prospectus dated August 12, 2015

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You should rely only on the information contained in this prospectus, the documents incorporated by reference 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 and the documents incorporated by reference is accurate only as of the date on the front cover of this prospectus, or such documents, as applicable, regardless of the time of delivery of this prospectus, such documents or any sale of shares of our common stock. 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 the documents incorporated by reference herein 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 incorporated by reference herein. 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," appearing elsewhere in this prospectus or incorporated by reference herein. 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 and other diseases of the eye. 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 existing therapies, with a favorable safety and tolerability profile at all doses tested. Our completed Phase 2 trial of *trabodenoson* co-administered with *latanoprost*, a prostaglandin analogue, or PGA, demonstrated IOP-lowering in patients who have previously had inadequate responses to treatment with *latanoprost*. These patients represent PGA poor-responders, as evidenced by persistently elevated IOP at levels that typically require the addition of a second drug to further lower IOP.

We had an End-of-Phase 2 meeting with the U.S. Food and Drug Administration, or 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. At the meeting, we reached agreement on the design of our initial Phase 3 trial, as well as the overall regulatory path for trabodenoson. For our first Phase 3 trial, we agreed to three doses of trabodenoson to be tested against placebo as the primary comparator for statistical purposes. We plan to start this trial for trabodenoson monotherapy in the fourth quarter of 2015 and expect to report top-line data from this trial by late 2016. We are also planning to complete a long-term safety trial using the highest

anticipated *trabodenoson* dose in late 2018. If the primary objectives of our Phase 3 program are met by all of our anticipated Phase 3 trials, we plan to submit a New Drug Application, or NDA.

Additionally, we are evaluating the potential for *trabodenoson* to directly target optic neuropathies. We are planning pre-clinical trials for optic neuropathies and degenerative retinal diseases beginning in the second half of 2015.

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. 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 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. As 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 the aqueous humor, the fluid in the eye, 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 monotherapy treatment in a Phase 2 clinical trial in glaucoma patients receiving no medications, *trabodenoson* (500 mcg) lowered IOP by 4.0 to 7.0 mmHg from study baseline, and 3.5 to 5.0 mmHg from diurnal 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 four 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 multiple-dose monotherapy 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 four weeks, even at the highest dose tested. Furthermore, in our most recently completed multiple-dose Phase 2 trial of *trabodenoson* co-administered with *latanoprost* in a population of PGA poor-responders, there also was no change in the rate of hyperemia from study baseline after four, eight or 12 weeks of treatment. 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 complementary mechanism was confirmed in patients already receiving *latanoprost* therapy in a recently completed multiple-dose Phase 2 trial. In this Phase 2 trial of *trabodenoson* co-administered with *latanoprost* in a population of PGA poor-responders, patients on *latanoprost* experienced an additional 5.5 mmHg IOP lowering from study baseline and 4.3 mmHg from diurnal baseline after 12 weeks of

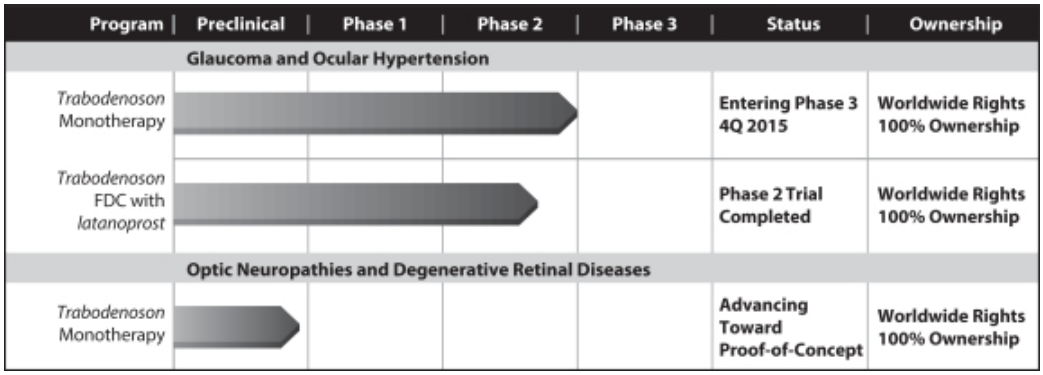
treatment (eight weeks BID plus four weeks QD). These results make *trabodenoson*, with its favorable safety profile, a candidate to add to other glaucoma medications when a further reduction of the IOP is desirable.

- **Convenient Dosing.** Current Phase 2 clinical data indicate that QD dosing with *trabodenoson* in PGA poor-responders is well tolerated and lowers IOP significantly. 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* IOP-lowering results, complementary mechanism of action, dosing profile and safety profile to date also make it well-suited for use in an FDC with a PGA, which could be a 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 neuropathies and degenerative retinal diseases. 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 to date 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, based on our completed Phase 2 study in which *trabodenoson* therapy was added to *latanoprost*, we believe that an FDC containing a PGA and *trabodenoson* 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 from our completed Phase 2 trial in which *trabodenoson* and *latanoprost* were co-administered. We believe that *trabodenoson*'s mechanism for lowering IOP complements 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 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 and Degenerative Retinal Diseases

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 neuropathies. We are planning pre-clinical trials for optic neuropathies and degenerative retinal diseases beginning in the second half of 2015.

Clinical Development Plan

We had an End-of-Phase 2 meeting with the FDA in the first half of 2015 to discuss our Phase 3 program for trabodenoson monotheraphy, and to confirm the design and endpoints for the Phase 3 pivotal trials. At the meeting, we reached agreement on the design for our initial Phase 3 study, as well as the overall regulatory path for *trabodenoson.* The trial design for the initial Phase 3 study is a five-arm superiority trial that will include three doses of *trabodenoson.* The doses were selected to optimize lowering of intraocular pressure while maintaining the good tolerability observed in the prior trials. The primary endpoint of the study is intraocular pressure (IOP), determined at several timepoints, during the day, after 4, 6 and 12 weeks of treatment. The IOP of the trabodenoson treated subjects will be statistically compared to the IOP of placebo treated subjects. A timolol arm will be included for study validation but not for statistical comparison.

We plan to start our Phase 3 program for *trabodenoson* monotherapy in the fourth quarter of 2015 and expect to report top-line data from the first pivotal trial in the program by late 2016.

After completion of a second pivotal trial and the long-term monotherapy safety study, if successful, we plan to submit an NDA to the FDA. We are planning to continue our Phase 2 program for our FDC in 2016 and to commence our Phase 3 program for our FDC in early 2018.

Our Strategy

Our goal is to become a leading biopharmaceutical company focused on the discovery, development and commercialization of novel therapies to treat glaucoma and other diseases of the eye. 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 and degenerative retinal diseases or for additional ophthalmic indications.

Recent Developments

- In July, we announced the Phase 3 development plan for *trabodenoson* based on a positive End-of-Phase 2 meeting with the FDA. The trial design for the first Phase 3 study is a five-arm superiority trial that will include three doses of *trabodenoson*: 1000 mcg QD, 1500 mcg BID, and 2000 mcg QD. These doses were selected to optimize lowering of intraocular pressure while maintaining the good tolerability observed in Phase 2 trials. The primary efficacy endpoint of the study is the reduction of IOP, statistically superior as compared to placebo. An arm of timolol will also be included for study validation, but not for statistical comparison.
- In July, we appointed Claudine Prowse, Ph.D., as Vice President, Strategy and Investor Relations Officer, and Cadmus Collins Rich, M.D., as Vice President, Medical Affairs and Clinical Development.
- In July, we appointed Richard N. Spivey, PharmD, Ph.D., to our Board of Directors.
- On August 6, 2015, we announced results for the second quarter of 2015. Our cash and cash equivalents as of June 30, 2015, were $49.0 million. Our research and development expenses were $2.0 million for the quarter ended June 30, 2015, compared to $1.9 million for the quarter ended June 30, 2014, and $3.0 million for the six months ended June 30, 2015, compared to $3.4 million for the six months ended June 30, 2014. Our general and administrative expenses were $1.7 million for the quarter ended June 30, 2015, compared to $0.3 million for the quarter ended June 30, 2014, and $3.7 million for the six months ended June 30, 2015, compared to $0.5 million for the six months ended June 30, 2014. Our net loss was $2.4 million for the quarter ended June 30, 2015, compared to a net loss of $2.8 million for the quarter ended June 30, 2014, and $3.8 million for the six months ended June 30, 2015, compared to $5.0 million for the six months ended June 30, 2014. Please see our financial statement for the six months ended June 30, 2015, which are incorporated herein by reference.

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 and the documents incorporated by reference herein. 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	5,400,000 shares of our common stock
Option to purchase additional shares	810,000 shares of our common stock
Common stock to be outstanding immediately after this offering	26,400,394 shares if the underwriters exercise their option to purchase additional shares
Use of proceeds	We estimate that we will receive net proceeds from this offering of approximately $64.2 million, or $73.9 million if the underwriters exercise their overallotment option, based on the public offering price of $12.75 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable. 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.
NASDAQ Global Market symbol	“ITEK”

The number of shares of our common stock to be outstanding after this offering is based on and includes (i) 16,327,003 shares of our common stock outstanding as of June 30, 2015, and (ii) 3,863,391 shares of common stock issued pursuant to the conversion of $21,000,000 principal amount of the 2020 Convertible Notes through August 7, 2015, which includes 3,333,319 shares related to the underlying 2020 Convertible Notes and 530,072 shares issued pursuant to the interest make-whole provision, which the Company elected to settle in shares, and excludes:

- 1,394,075 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2015 at a weighted-average exercise price of $4.92 per share; and
- 56,408 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2015, which have an exercise price of $6.204 per share.

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

- no issuance or exercise of stock options or warrants after June 30, 2015; and
- no exercise by the underwriters of their option to purchase up to an additional 810,000 shares of common stock in this offering.

Summary Financial Data

The selected statements of operations data for the years ended December 31, 2013 and 2014 and the balance sheet data as of December 31, 2013 and 2014, have been derived from our audited consolidated financial statements incorporated by reference in this prospectus from our Annual Report on Form 10-K. The selected statements of operations data for the six months ended June 30, 2014 and 2015, and the balance sheet data as of June 30, 2015, have been derived from our unaudited financial statements incorporated by reference in this prospectus from our Quarterly Report for the quarterly period ended June 30, 2015. 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 as well as the information under the captions "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2014, and our Quarterly Report on Form 10-Q for the quarter ended June 30, 2015, incorporated herein by reference. Our historical results are not necessarily indicative of our future results, and results for the six-month period ended June 30, 2015, are not necessarily indicative of the results to be expected for the year ending December 31, 2015, or any other interim periods or any future year or period.

	Year Ended December 31,		Six Months Ended June 30,	
	2013	2014	2014	2015
(in thousands, except share and per share data)			(unaudited)	
Statements of Operations Data:				
Operating expenses:				
Research and development	$ (5,330)	$ (5,592)	$ (3,412)	$ (3,023)
General and administrative	(1,324)	(2,112)	(494)	(3,708)
Loss from operations	(6,654)	(7,704)	(3,906)	(6,731)
Other income	3	–	–	–
Interest expense	(884)	(980)	(491)	(1,038)
Loss on extinguishment of debt	–	–	–	(683)
Change in fair value of 2020 Notes derivative liability	–	–	–	3,856
Change in fair value of Convertible Bridge Notes redemption rights derivative	–	–	–	480
Change in fair value of warrant liabilities	(81)	(847)	(598)	267
Net loss	$ (7,616)	$ (9,531)	$ (4,995)	$ (3,849)
Net loss per common share—basic and diluted	$ (10.05)	$ (13.52)	$ (6.89)	$ (0.33)
Weighted-average common shares outstanding—basic and diluted	1,018,183	1,020,088	1,020,088	12,026,183

(in thousands)	Year Ended December 31, 2013	Year Ended December 31, 2014	June 30, 2015 (unaudited)
Balance Sheet Data:			
Cash and cash equivalents	$ 12,793	$ 3,618	$ 49,012
Total assets	12,863	5,520	51,688
Convertible Bridge Notes	–	1,541	–
2020 Convertible Notes	–	–	8,926
Notes payable, current portion	1,410	3,063	–
Notes payable, net of current portion	5,395	2,550	–
Warrant liabilities and Convertible Bridge Notes redemption rights derivative	1,888	962	–
2020 Convertible Notes derivative liability	–	–	8,567
Total liabilities	10,525	10,278	19,969
Series AA redeemable convertible preferred stock	40,685	46,253	–
Accumulated deficit	(118,510)	(128,041)	(131,890)
Total stockholders' equity (deficit)	(38,895)	(51,559)	31,719

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 and in the documents incorporated by reference herein 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 $9.5 million and $7.6 million for the years ended December 31, 2014 and 2013, respectively. Our net losses were $3.8 million and $5.0 million for the six months ended June 30, 2015 and 2014, respectively. As of June 30, 2015, we had an accumulated deficit of $131.9 million.

Investment in pharmaceutical product development is highly speculative because it entails substantial upfront 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 stock. 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. In December 2014, we completed the issuance and sale of $2.0 million of subordinated convertible promissory notes. Our product candidates will require the completion of regulatory review, significant marketing efforts and substantial investment before they can provide us with any revenue.

In February 2015, we completed our initial public offering of 6,667,000 shares of our common stock at a price of $6.00 per share and a concurrent offering of $20.0 million aggregate principal amount of 5.0% Convertible Senior Notes due in 2020 (the “2020 Convertible Notes”). In March 2015, the underwriters exercised 299,333 shares of common stock at $6.00 per share and $1.0 million of the 2020 Convertible Notes pursuant to their overallotment options. We received net proceeds of approximately $36.5 million, after deducting underwriting discounts and offering-related costs, from our equity issuances and approximately $18.9 million in net proceeds, after deducting underwriting discounts and offering-related costs, from our debt issuances.

We expect our research and development expenses to continue to be significant in connection with our product development activities, including our planned Phase 2 clinical trials and our planned Phase 3 programs. 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, 2015, our cash and cash equivalents were $49.0 million. We estimate that the net proceeds to us from the sale of 5,400,000 shares of common stock in this offering will be approximately $64.2 million, based upon an offering price of $12.75 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We believe that the net proceeds from this offering of common stock, together with existing cash and cash equivalents, will be sufficient to fund our projected operating requirements for at least the next 24 months. We will need to obtain additional financing to conduct additional trials for the approval of our drug candidates 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 potential 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, the agreements that govern our existing indebtedness contain covenants that restrict our ability to incur additional indebtedness and incur certain liens, for example.

We may require additional capital to operate or expand our business. 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 develop and 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 develop and 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 upcoming pivotal trials of *trabodenoson* monotherapy or our upcoming continuing Phase 2 program for the FDC product candidate 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. We have completed a Phase 2 trial in which we tested *trabodenoson* co-administered with *latanoprost*. We attended 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 the fourth quarter of 2015, which will consist of two Phase 3 pivotal trials and a long-term safety study. We cannot predict whether any of our 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. Moreover, determination of the ultimate study design and its confirmation with the FDA could result in a significant range of costs for the Phase 3 pivotal trials.

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. To complete the studies for our product candidates, we will require additional 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.

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 recently completed 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 any 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 233 clinical trial subjects to *trabodenoson*. The FDA expects that a total of at least 1,300 patients will be 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, and IRBs may at any time order or data safety monitoring boards may at any time recommend to the sponsor 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 planned Phase 3 pivotal trials of *trabodenoson* monotherapy may not produce the results that we expect. Our planned 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 systemic 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 approved 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. If approved, 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 cGMP. 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;
- differing reimbursement regimes and price controls in certain non-U.S. markets;
- 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 degree to which our product candidates obtain coverage and adequate reimbursement;
- 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 primarily includes 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 or entity, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration, directly or indirectly, in cash or in kind, that is intended to induce or reward 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, many healthcare fraud and abuse laws are broadly written, and it may be 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 and civil monetary penalties laws, including the civil False Claims Act prohibits any individual or entity 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, or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government. The civil False Claims Act 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. 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 civil 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.

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 for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, report annually to the Centers for Medicare & Medicaid Services, or CMS, 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, including state anti-kickback and false claims 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 may be 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 on certain types of individuals and organizations. 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, many state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other and from HIPAA 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, among other things, 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. Among other changes that affect the pharmaceutical industry, 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% point-of-sale discount off the negotiated price of applicable 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 2012 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 glaucoma, other neuropathies and degenerative retinal diseases.

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 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, 2015, we own at least 50 issued patents and have at least 40 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 eleven full-time employees as of July 31, 2015, 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.

We are 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 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 manufacturers 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.

The availability of our common stock and securities linked to our common stock for sale in the future could reduce the market price of our common stock.

In the future, we may issue equity and equity-linked securities to raise cash for acquisitions or otherwise. We may also acquire interests in other companies by using a combination of cash and our common stock or just our common stock. We may also issue preferred stock or additional securities convertible into our common stock or preferred stock. Any of these events may dilute your ownership interest in our Company and have an adverse effect on the price of our common stock.

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 offering price.

Our initial public offering was completed in February 2015. Therefore, there has only been a public market for our common stock for a short period of time. Although our common stock is listed on NASDAQ, if an active trading market for our common stock may not develop or continue following this offering, and you may not be able to sell your shares quickly or above the offering price.

The trading price of our common stock is likely to continue to be volatile, and you can lose all or part of your investment in us. 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;
- sales by us of securities linked to our common stock, such as the 2020 Convertible Notes;
- 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, a significant decline in the financial markets and other 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 has been and may continue to 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.

As of June 30, 2015, our officers and directors, and stockholders who own more than 5% of our outstanding common stock, in the aggregate, beneficially owned approximately 75% of our common stock.

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 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 $8.38 per share, based on the offering price of $12.75 per share and our pro forma net tangible book value as of June 30, 2015.

In the past, we have issued options and warrants to acquire shares of our capital stock at prices significantly below the 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 or any of our securities linked to our common stock, such as the 2020 Convertible Notes, 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 or equity-linked securities. Substantially all of our stockholders prior to our initial public offering are subject to lock-up agreements with the underwriters of our initial public offering that restrict the stockholders’ ability to transfer shares of our common stock for a period of 180 days after the pricing date of the initial public offering, February 17, 2015, or the IPO Lock Up Period. Certain of our officers, directors and such directors’ affiliates are subject to lock-up agreements with the underwriters of this offering that restrict their ability to transfer shares of our common stock for a period of 90 days after the date of this prospectus, or the Current Lock-Up Period.

After this offering, we will have 25,590,394 outstanding shares of common stock based on and including (i) 16,327,003 shares of our common stock outstanding as of June 30, 2015, and (ii) 3,863,391 shares of common stock issued pursuant to the conversion of $21,000,000 principal amount of the 2020 Convertible Notes through August 7, 2015, which includes 3,333,319 shares related to the underlying 2020 Convertible Notes and 530,072 shares issued pursuant to the interest make-whole provision, which the Company elected to settle in shares, and excludes:

- 1,394,075 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2015 at a weighted-average exercise price of $4.92 per share; and
- 56,408 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2015, which have an exercise price of $6.204 per share.

Subject to limitations, approximately 3.3 million shares will become eligible for sale upon expiration of the IPO Lock-Up Period and approximately 8.7 million shares will become eligible for sale upon the expiration of the Current Lock-Up Period, such number of shares 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 and based on the number of shares outstanding at June 30, 2015, holders of an aggregate of 8.8 million 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, 2014, we had federal and state net operating losses of approximately $77 million and $36 million, respectively, which may be utilized against future federal and state income taxes, respectively. 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 fifty percentage points 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 are beyond our control, or prior issuances of our common stock, could create a limitation on our ability to utilize our NOLs for tax purposes in the future, including by the issuance of common stock pursuant to this offering. Limitations imposed on our ability to utilize NOLs could cause 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, or have occurred in the past, 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 require significant company resources and management attention.

We are 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 incur substantial legal, accounting and other expenses. Further, 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 increased costs as a result of operating as a public company, and our management team will be required to devote substantial time to new compliance initiatives.

Now that we are a public company, and particularly after we are no longer considered an “emerging growth company,” we will incur significant legal, accounting and other expenses that we did

not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the Securities and Exchange Commission and The NASDAQ Stock Market have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. 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.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our consolidated financial statements.

The 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) December 31, 2020; (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 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 and the documents incorporated by reference herein 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 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 or incorporated by reference herein 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 and the documents incorporated by reference herein 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 and the documents incorporated by reference herein 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 documents incorporated by reference 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 and the documents incorporated by reference herein 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 5,400,000 shares of common stock in this offering will be approximately $64.2 million based upon the public offering price of $12.75 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters' exercise their option to purchase additional shares, we estimate that our net proceeds will be approximately $73.9 million, after deducting 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, and for general corporate purposes. We currently expect to use the net proceeds from this offering as follows:

- approximately $9.0 million to complete the second Phase 3 pivotal trial for *trabodenoson* monotherapy, including associated payments for direct clinical and non-clinical costs;
- approximately $18.0 million to initiate enrollment of a Long-Term Safety Study, the third Phase 3 trial required for filing the *trabodenoson* monotherapy NDA, including associated direct clinical and non-clinical costs;
- approximately $4.0 million to initiate a Phase 3 trial of our FDC product candidate, including associated payments for direct clinical and non-clinical costs; and
- the remainder for working capital and general corporate purposes.

Based on our current plans, we believe our cash, cash equivalents and short-term investments, together with the proceeds to us from this offering will be sufficient to fund our operations for at least the next 24 months.

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. For example, the ultimate cost of clinical trials depends on trial designs that must be confirmed with the FDA and can vary significantly. 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.

PRICE RANGE OF COMMON STOCK

Our common stock began trading on The NASDAQ Global Market under the symbol “ITEK” on February 18, 2015. Prior to that time, there was no public market for our common stock. The following table sets forth the high and low sale prices per share of our common stock, as reported on The NASDAQ Global Market, for the periods indicated.

	High	Low
Year Ending December 31, 2015		
First quarter	$ 6.20	$5.05
Second quarter	$ 6.14	$4.68
Third quarter (through August 12, 2015)	$19.45	$4.71

On August 12, 2015, the last reported sale price of our common stock as reported on The NASDAQ Global Market was $13.50 per share. As of June 30, 2015, we had 52 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

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, 2015:

- on an actual basis;
- on a pro forma basis to give effect to 3,863,391 shares of common stock issued pursuant to the conversion of $21,000,000 principal amount of the 2020 Convertible Notes through August 7, 2015, which includes 3,333,319 shares related to the underlying 2020 Convertible Notes and 530,072 shares issued pursuant to the interest make-whole provision, which the Company elected to settle in shares; and
- on a pro forma as adjusted basis to give further effect to our sale in this offering of 5,400,000 shares of common stock at the public offering price of $12.75 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

You should read the following table together with the sections titled “Use of Proceeds,” “Selected Financial Data,” “Description of Capital Stock” and the financial statements and related notes appearing elsewhere in this prospectus and the documents incorporated by reference herein.

	As of June 30, 2015		
(in thousands, except share and per share amounts)	Actual (unaudited)	Pro Forma (unaudited)	Pro Forma, as adjusted (unaudited)
Cash and cash equivalents	$ 49,012	$ 49,012	$ 113,231
2020 Convertible Notes	$ 8,926	$ –	$ –
Stockholders’ equity:			
Common stock, $0.01 par value; 120,000,000 shares authorized; 16,327,003 shares issued and outstanding, actual; 20,190,394 shares issued and outstanding, pro forma; 25,590,394 shares issued and outstanding, pro forma as adjusted	163	202	256
Additional paid-in capital	163,446	229,781	293,946
Accumulated deficit	(131,890)	(182,443)	(182,443)
Total stockholders’ equity	31,719	47,540	111,759
Total capitalization	$ 40,645	$ 47,540	$ 111,759

The above discussion and tables are based on and include (i) 16,327,003 shares of our common stock issued and outstanding as of June 30, 2015, and (ii) 3,863,391 shares of common stock issued pursuant to conversion of $21,000,000 principal amount of the 2020 Convertible Notes through August 7, 2015, which includes 3,333,319 shares related to the underlying 2020 Convertible Notes and 530,072 shares issued pursuant to the interest make-whole provision, which the Company elected to settle in shares, and excludes:

- 1,394,075 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2015 at a weighted-average exercise price of $4.92 per share; and
- 56,408 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2015, which have an exercise price of $6.204 per share.

DILUTION

If you invest in our common stock in this offering, your interest will be diluted to the extent of the difference between the 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, 2015 was $31.7 million, or $1.94 per share, based on 16,327,003 shares of common stock outstanding as of June 30, 2015.

The pro forma net tangible book value of our common stock as of June 30, 2015 was $47.5 million, or approximately $2.35 per share of common stock, based on 16,327,003 shares of our common stock outstanding, after giving effect to the conversion of the $21.0 million principal amount of 2020 Convertible Notes into 3,863,391 shares of common stock.

After giving further effect to our sale of 5,400,000 shares in this offering at the public offering price of $12.75 per share, after deducting underwriting discounts and commissions and estimated offering expenses, our pro forma net tangible book value as of June 30, 2015 would be $111.8 million, or $4.37 per share. This represents an immediate increase in net tangible book value of $2.02 per share to existing stockholders and an immediate dilution in net tangible book value of $8.38 per share to purchasers of common stock in this offering, as illustrated in the following table:

Public offering price per share		$12.75
Historical net tangible book value per share as of June 30, 2015	$1.94	
Increase attributable to the proforma transaction described above, before giving effect to this offering	0.41	
Proforma net tangible book value per share as of June 30, 2015	2.35	
Increase in net tangible book value per share attributable to new investors purchasing shares in this offering	2.02	
Pro forma as adjusted net tangible book value per share at June 30, 2015 after giving effect to this offering		4.37
Dilution per share to new investors participating in this offering		$ 8.38

If the underwriters exercise their option to purchase additional shares, the pro forma as adjusted net tangible book value would be $4.60 per share, and the dilution in pro forma as adjusted net tangible book value to investors in this offering would be $8.15 per share. The following table summarizes, on a pro forma as adjusted basis as of June 30, 2015, 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 and by investors participating in this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, at the public offering price of $12.75 per share.

	Shares Purchased		Total Consideration		Average price / share
	Number	Percent	Amount	Percent	
Existing stockholders	20,190,394	79%	$184,545,000	73%	$ 9.14
New investors	5,400,000	21%	68,850,000	27%	$ 12.75
Total	25,590,394	100%	$253,395,000	100%	$ 9.90

The above discussion and tables are based on (i) 16,327,003 shares of common stock issued and outstanding as of June 30, 2015, and (ii) 3,863,391 shares of common stock issued pursuant to the conversion of $21,000,000 principal amount of the 2020 Convertible Notes, plus the interest make-whole amount of $3,070,000, which the Company elected to settle in shares, through August 7, 2015, which includes 3,333,319 shares related to the underlying 2020 Convertible Notes and 530,072 shares issued pursuant to the interest make-whole provision, which the Company elected to settle in shares, and excludes:

- 1,394,075 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2015, at a weighted-average exercise price of $4.92 per share; and
- 56,408 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2015, which have an exercise price of $6.204 per share.

If the underwriters exercise their option to purchase additional shares, the number of shares of common stock held by existing stockholders will be reduced to 76% 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

The selected statements of operations data for the years ended December 31, 2013 and 2014, and the balance sheet data as of December 31, 2013 and 2014, have been derived from our audited financial statements incorporated by reference in this prospectus from our Annual Report on Form 10-K for the fiscal year ended December 31, 2014. The selected statements of operations data for the six months ended June 30, 2014 and 2015, and the balance sheet data as of June 30, 2015, have been derived from our unaudited financial statements incorporated by reference in this prospectus from our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2015. 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 and the information under the caption "Management's Discussion and Analysis of Financial Condition and Results of Operations" incorporated by reference herein. Our historical results are not necessarily indicative of our future results, and results for the six-month period ended June 30, 2015, are not necessarily indicative of the results to be expected for the year ending December 31, 2015, or any other interim periods or any future year or period.

	Year Ended December 31,		Six Months Ended June 30,	
	2013	2014	2014	2015
(in thousands, except share and per share data)			(unaudited)	
Statements of Operations Data:				
Operating expenses:				
Research and development	$ (5,330)	$ (5,592)	$ (3,412)	$ (3,023)
General and administrative	(1,324)	(2,112)	(494)	(3,708)
Loss from operations	(6,654)	(7,704)	(3,906)	(6,731)
Other income	3	–	–	–
Interest expense	(884)	(980)	(491)	(1,038)
Loss on extinguishment of debt	–	–	–	(683)
Change in fair value of 2020 Convertible Notes derivative liability	–	–	–	3,856
Change in fair value of Convertible Bridge Notes redemption rights derivative	–	–	–	480
Change in fair value of warrant liabilities	(81)	(847)	(598)	267
Net loss	$ (7,616)	$ (9,531)	$ (4,995)	$ (3,849)
Net loss per common share—basic and diluted	$ (10.05)	$ (13.52)	$ (6.89)	$ (0.33)
Weighted-average common shares outstanding—basic and diluted	1,018,183	1,020,088	1,020,088	12,026,183

(in thousands)	Year Ended December 31, 2013	Year Ended December 31, 2014	June 30, 2015 (unaudited)
Balance Sheet Data:			
Cash and cash equivalents	$ 12,793	$ 3,618	$ 49,012
Total assets	12,863	5,520	51,688
Convertible Bridge Notes	–	1,541	–
2020 Convertible Notes	–	–	8,926
Notes payable, current portion	1,410	3,063	–
Notes payable, net of current portion	5,395	2,550	–
Warrant liabilities and Convertible Bridge Notes redemption rights derivative	1,888	962	–
2020 Convertible Notes derivative liability	–	–	8,567
Total liabilities	10,525	10,278	19,969
Series AA redeemable convertible preferred stock	40,685	46,253	–
Accumulated deficit	(118,510)	(128,041)	(131,890)
Total stockholders' equity (deficit)	(38,895)	(51,559)	31,719

BUSINESS

Overview

We are a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of therapies for glaucoma and other diseases of the eye. 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. We are also evaluating the potential of *trabodenoson* to slow the loss of vision associated with glaucoma and degenerative retinal diseases. 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 existing therapies, with a favorable safety and tolerability profile at all doses tested. Our completed Phase 2 trial of *trabodenoson* co-administered with *latanoprost*, a prostaglandin analogue, or PGA, demonstrated IOP-lowering in patients who have previously had inadequate responses to treatment with *latanoprost*. These patients represent PGA poor-responders, as evidenced by persistently elevated IOP at levels that typically require the addition of a second drug to further lower IOP.

We had 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. At the meeting, we reached agreement on the design of our initial Phase 3 study, as well as the overall regulatory path for trabodenoson. We plan to start our Phase 3 program for trabodenoson monotherapy in the fourth quarter of 2015, and, based on our estimate of the rate of patient enrollment, we expect to report top-line data from the first pivotal trial in the program by late 2016. If the primary objectives of all of the trials in 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. 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 *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 had 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. At the meeting, we reached agreement on the design of our initial Phase 3 study, as well as the overall regulatory path for trabodenoson. Based on our estimates of the rate of patient enrollment and assuming commencement in the fourth quarter of 2015, we expect to have top-line data from the initial Phase 3 trial by late 2016. 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. Our completed Phase 2 trial of *trabodenoson* co-administered with the

PGA, *latanoprost*, demonstrated IOP-lowering in patients who have previously had inadequate responses to the PGA, *latanoprost*. These patients represent PGA poor-responders, as evidenced by persistently elevated IOP at levels that typically require the addition of a second drug to further lower IOP.

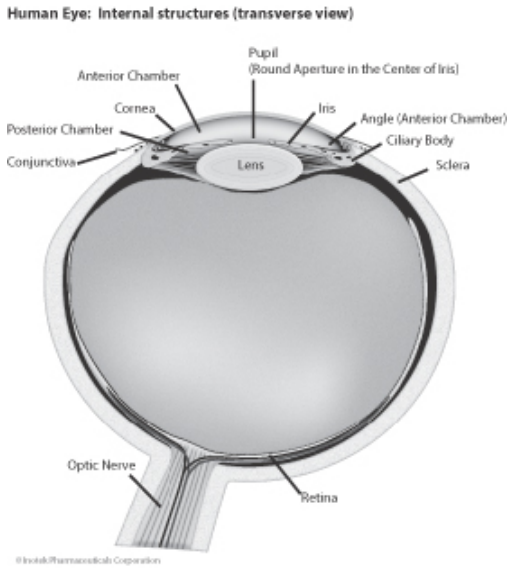
- ***Establish a specialty sales force to maximize the commercial potential of trabodenoson in the United States***. We have retained worldwide commercial rights to *trabodenoson*. If *trabodenoson* receives marketing approval in the United States, we plan to commercialize it by establishing a glaucoma-focused 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 and degenerative retinal diseases 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. To begin this process, we will be conducting pre-clinical trials for optic neuropathies and degenerative retinal diseases starting in the second half of 2015.

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.

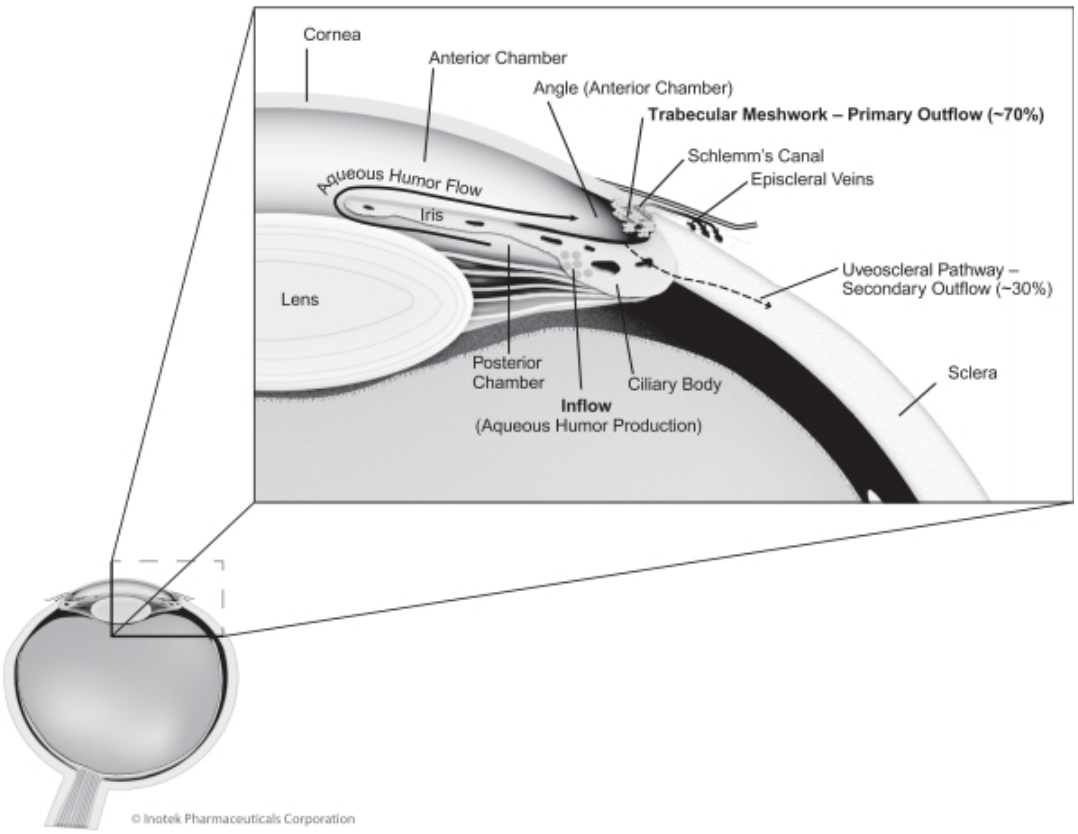
Physiology of the Eye

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 focus 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:



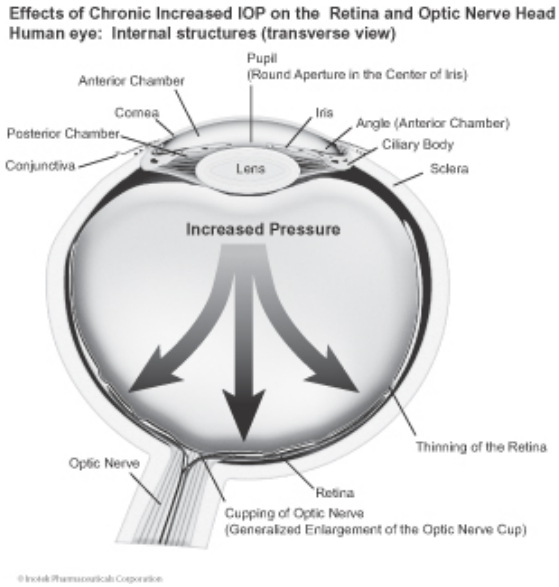
In this angle, in front of the outer rim of the iris, is the TM, a natural, pressure-regulating drain. It is here that in a healthy, well-functioning eye, approximately 70% of the aqueous humor exits and flows into a drainage canal known as Schlemm's canal, which empties back into the venous drainage 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

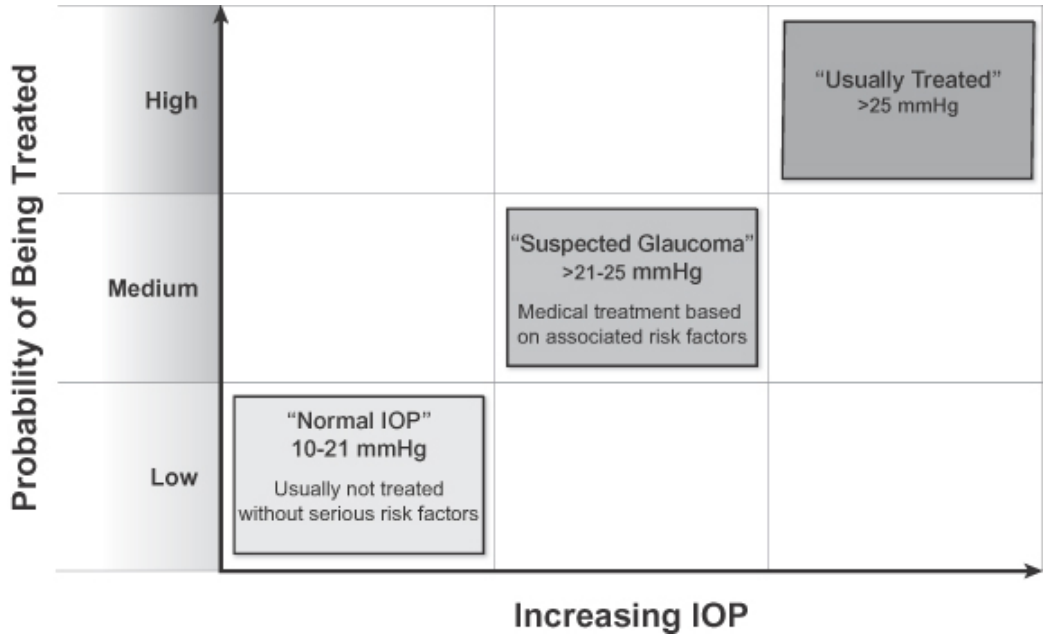
In a typical glaucoma patient, there is resistance to drainage of the aqueous fluid (i.e., not enough aqueous humor exits the eye), creating excess pressure and compressing the retina, the layer of tissue covering the inside of the back half of the eye that actually converts light into nerve impulses. 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 Guidelines, or 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. According to IMS Health, approximately two-thirds 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.

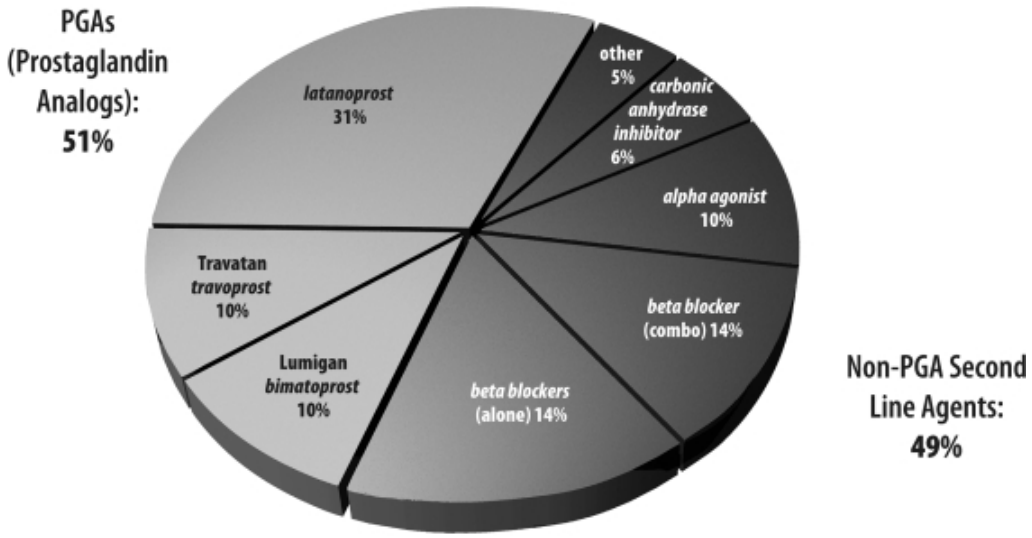
The existing classes of treatment available for glaucoma each have varying mechanisms of action, levels of IOP-lowering, side effects and other adverse effects, as described in the following table.

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.

A Rho kinase inhibitor recently entered Phase 3 clinical trials and is the furthest along of the potential new glaucoma therapies: Aerie Pharmaceuticals, Inc.'s AR-13324. 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, the fluid in the eye, 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 monotherapy treatment in a Phase 2 clinical trial in glaucoma patients who had discontinued any other medications, *trabodenoson* (500 mcg) lowered IOP by an average of 4.0 to 7.0 mmHg from study baseline and 3.5 to 5.0 mmHg from diurnal baseline, over the dosing interval. Moreover, IOP-lowering at week four was significantly better than IOP-lowering at week two.
- **Favorable Safety Profile.** In four 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 multiple-dose Phase 2 monotherapy 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 four weeks, even at the highest dose tested. Furthermore, in our most recently completed multiple-dose Phase 2 trial of *trabodenoson* co-administered with *latanoprost* in a population of PGA poor-responders, there also was no change in the rate of hyperemia from study baseline after four, eight or 12 weeks of treatment. 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 complementary mechanism was confirmed in patients already receiving *latanoprost* therapy in a recently completed multiple-dose Phase 2 trial. In this Phase 2 trial of *trabodenoson* co-administered with *latanoprost* in a population of PGA poor-responders, patients on *latanoprost* experienced an additional 5.8 mmHg IOP lowering from their study baseline and 4.3 mmHg from their diurnal baseline after 12 weeks treatment (eight weeks BID plus four weeks QD). These results make *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 Phase 2 clinical data indicate that QD dosing with *trabodenoson* in PGA poor-responders is well tolerated and lowers IOP significantly. 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 and approved in our Phase 3 program, QD dosing would make *trabodenoson* easier to use than most non-PGA

products, and *trabodenoson*'s dosing frequency would match the best-in-class PGAs, which would facilitate an FDC with a PGA that could be dosed QD.

We believe that *trabodenoson*'s IOP-lowering results, complementary mechanism of action, dosing and safety profile make it well suited for use in an FDC with a PGA, which could be a 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	
				A2a/A1	A3/A1
Trabodenoson	0.97	4,690	704	4,835x	725x

Trabodenoson's *key characteristics include:*

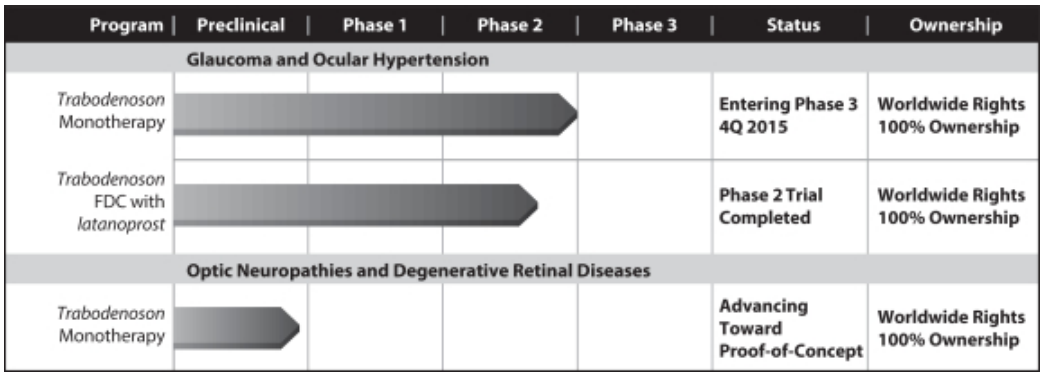
1. Potency—Ki in single-digit nM range (0.97nM);
2. High Selectivity—over A2a> 1000-fold and A3>500-fold;
3. Ease of Fat Solubility—allowing corneal penetration so it can reach the TM; and
4. A high compatibility with the often sensitive tissues in the front of the eye.

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 neuropathies and degenerative retinal diseases. 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, based on our completed Phase 2 study in which *trabodenoson* therapy was co-administered with *latanoprost*, we believe that an FDC containing a PGA and *trabodenoson* 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 from our completed Phase 2 trial in which *trabodenoson* and *latanoprost* were co-administered. We believe that

trabodenoson's mechanism for lowering IOP complements 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.

Our completed Phase 2 trial of *trabodenoson* co-administered with *latanoprost* also demonstrated IOP-lowering in patients who have previously had inadequate responses to *latanoprost*. These patients represent PGA poor-responders, as evidenced by persistently elevated IOP at levels that typically require the addition of a second drug to further lower IOP. The safety profile of *trabodenoson* co-administered with *latanoprost* is similar to that of *trabodenoson* monotherapy. Moreover, *trabodenoson* had a sufficiently long duration of action, allowing it to be effectively dosed QD in conjunction with *latanoprost*. 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 and Degenerative Retinal Diseases

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. A pre-clinical study of the impact of high IOP on RGCs showed that *trabodenoson* could protect this key population of cells in the retina that, when lost, result in the irreversible vision loss associated with glaucoma. 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 neuropathies.

Clinical Data and Development Strategy

Our Phase 3 program for *trabodenoson* as a monotherapy will incorporate the FDA-acceptable clinical endpoint of IOP, in studies with three months of treatment. We had 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. At the meeting, we reached agreement on the design for our initial Phase 3 study, as well as the overall regulatory path for trabodenoson. The trial design for the initial Phase 3 study is a five-arm superiority trial that will include three doses of trabodenoson. The primary endpoint of the study is intraocular pressure (IOP), determined at four timepoints during the day, after 4, 6 and 12 weeks of treatment. The IOP of the trabodenoson treated subjects will be statistically compared to those of placebo treated subjects. A timolol arm will be included for study validation, but not for statistical comparison.

We plan to start our Phase 3 program for *trabodenoson* monotherapy in the fourth quarter of 2015, and we expect to report top-line data from the first pivotal trial in the program by late 2016. If the primary objectives of all of the trials in 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 early 2018.

Clinical Results

Trabodenoson Phase 2 Tolerability, Safety and Efficacy of Monotherapy in Glaucoma Patients

In 2012, we completed a successful Phase 2 dose-ranging clinical trial in 144 patients with OHT (ocular hypertension with no visual field 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 two 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.

The primary efficacy endpoint was IOP (measured throughout the day). The primary efficacy analysis calculated the reduction in IOP from the patients' IOP at the beginning of the study (recorded before active drug was administered at the study 8 AM baseline). A second analysis calculated the reduction in IOP from a time-matched diurnal baseline. The 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.

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

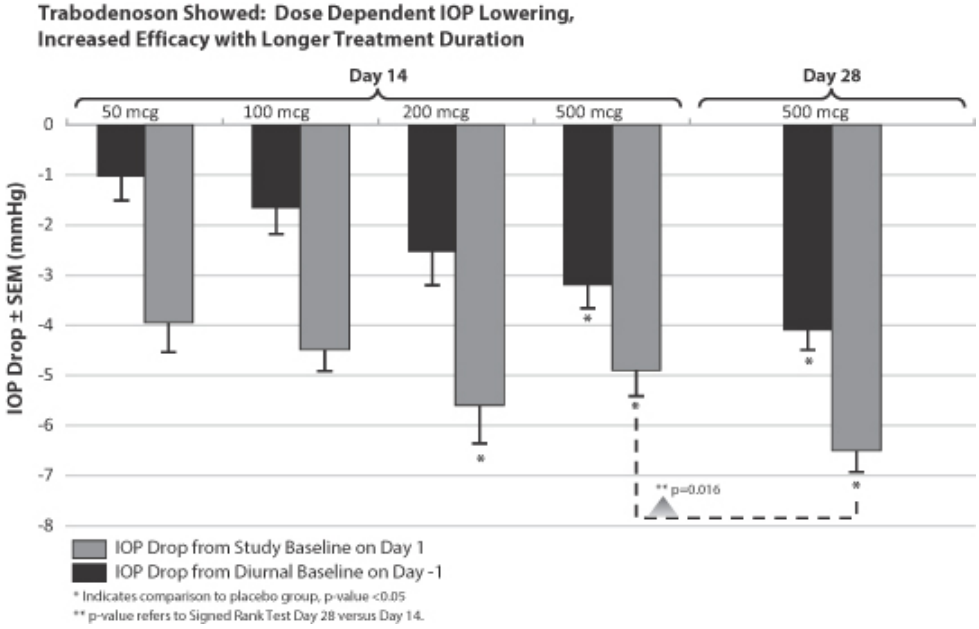
Patient Population: The characteristics of the patients in the dose groups were similar, including their ages, baseline IOPs, and diagnoses (OHT or POAG). The table below reflects information regarding the demographics of the patient populations that participated in the study, and shows that both diagnoses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

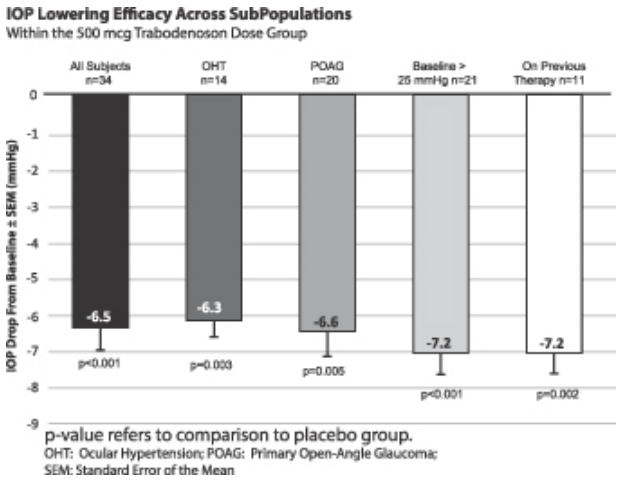
Efficacy

Both the 200 mcg dose and the 500 mcg doses at day 14, and the 500 mcg dose at 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 additional 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.

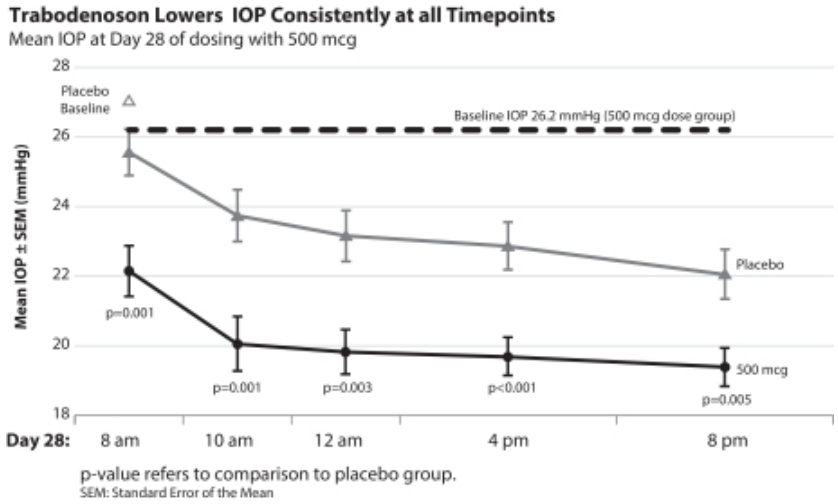


On average, doubling doses between 50 and 500 mcg increases IOP lowering from diurnal baseline by approximately 0.7 mmHg.

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 study 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 the primary efficacy parameter for the trial, IOP, at several timepoints throughout the day (diurnal IOP) for the highest dose tested and the placebo group 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 indicates the potential for *trabodenoson* monotherapy to be dosed QD.

Safety and Tolerability

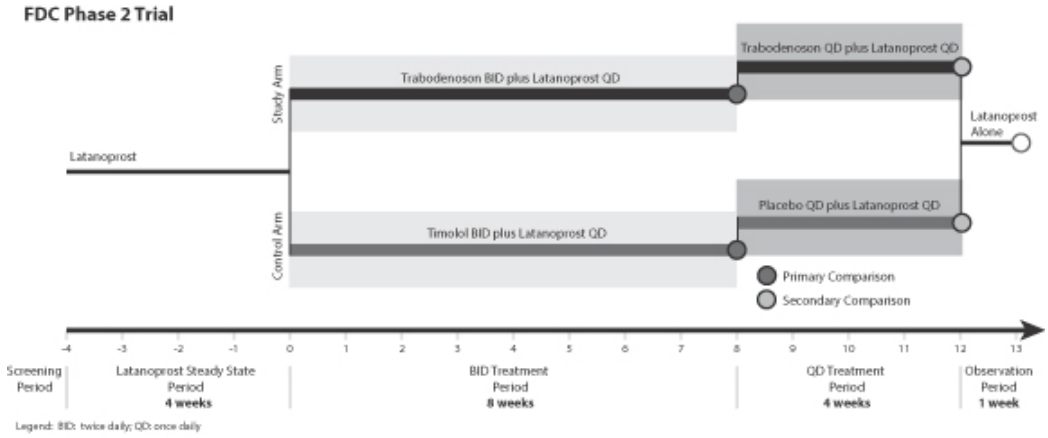
There were no serious adverse events or patients that withdrew due to safety findings that occurred once the drug was given. There were no signs of systemic safety issues in any of the non-ocular examinations, ECG evaluations or laboratory tests performed. Systemically, administration of *trabodenoson* 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 Phase 2 Co-Administered with Latanoprost in Glaucoma Patients

In October 2014, we received top-line results from a Phase 2 trial in patients with POAG or OHT, in which *trabodenoson* eye drops were co-administered with *latanoprost* eye drops. The objective of the study was to evaluate the safety and additional IOP-lowering effect of *trabodenoson* when added either BID or QD to *latanoprost*. This trial enrolled 101 patients who had IOPs of greater than or equal to 24 mmHg despite one month of previous treatment with *latanoprost*. These patients are considered PGA poor-responders, as evidenced by persistently elevated IOP at levels that typically require the addition of a second drug to further lower IOP. The trial was randomized, double-masked, placebo- and active- controlled.

Following four weeks of *latanoprost* eye drops, otherwise healthy patients with an IOP greater than 24 mmHg and a diagnosis of either OHT or POAG were randomized for Part 1 of the study. In Part 1, the study arm consisted of BID-dosed *trabodenoson* (1.5%; 500 mcg nominal dose) plus *latanoprost* 0.005%, at the approved dose, QD. The control arm consisted of *timolol* 0.5%, an approved BID dose plus *latanoprost* 0.005% QD. Patients in both arms were treated for a total of eight weeks in Part 1 of the study to evaluate the additive effects of trabodenoson BID to *latanoprost* QD, with an active control consisting of *timolol* BID.

At the end of Part 1, after eight weeks of treatment, patients began Part 2 of the study. In Part 2, the study arm was switched to a QD dose of *trabodenoson* (3.0%, 1,000 mcg nominal dose) plus *latanoprost* 0.005% QD, and patients in the control arm were switched to placebo QD plus *latanoprost* 0.005% QD. Part 2 was designed to measure the additive effects of *trabodenoson* QD to *latanoprost* QD over an additional four weeks. The number of patients planned for enrollment was ~100 (50 patients per arm) for Part 1 and ~80 (40 patients per arm) for Part 2. This trial is outlined below.



The primary efficacy endpoint was IOP, measured throughout the day. The efficacy analyses calculated the reduction in IOP from the patients' IOP at study baseline and diurnal baseline (recorded after taking *latanoprost* for four weeks but before *trabodenoson* or *timolol* were added). In Part 1, these IOP drops from baseline, on *latanoprost,* were compared to the IOP drops of the control arm treated concurrently with *timolol*. In Part 2, the IOP drop from baseline in patients receiving *trabodenoson* QD plus *latanoprost* QD was compared to patients receiving placebo QD plus *latanoprost* QD.

Safety evaluations included recording of withdrawals or terminations and adverse events, or AEs. In each patient, both eyes were 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). 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 age, and baseline IOPs, which were not adequately controlled following a four-week run-in using *latanoprost* therapy. The table below includes information on the demographics of the patients that participated in the study.

Baseline Demographics and IOP

	Part 1		Part 2	
ITT population	***Trabodenoson* BID**	***Timolol* BID**	***Trabodenoson* QD**	**Placebo QD**
n	50	51	37	43
Mean Age	62	61	63	61
Baseline IOP using *latanoprost* (mmHg)	25.71	25.86	25.68	25.86
OHT n (%)	23(46%)	13(25.5%)	15(40.5%)	12(28%)
Baseline IOP using *latanoprost* (mmHg)	25.78	25.65	25.93	25.29
POAG n (%)	27(54%)	38(74.5%)	22(59.5%)	31(72%)
Baseline IOP using *latanoprost* (mmHg)	25.65	25.93	25.50	26.08

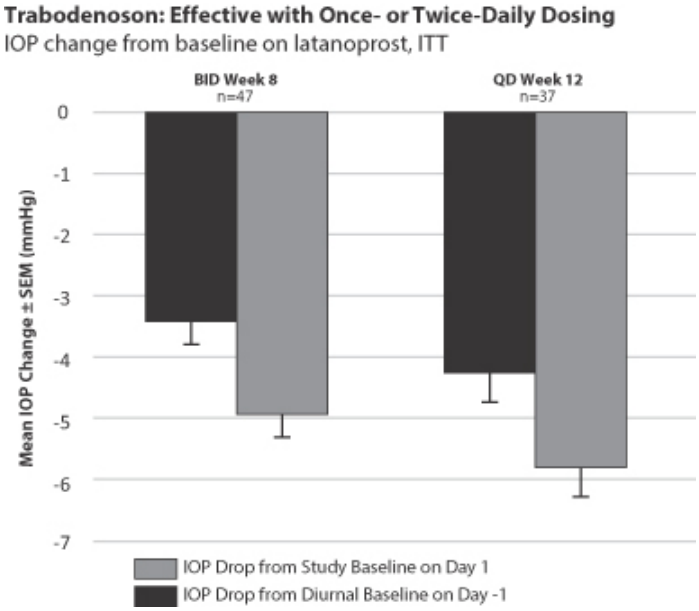
Discontinuations:

In Part 1, there were four discontinuations due to either protocol violations or exclusionary criteria (three patients were in the *trabodenoson* group and one was in the *timolol* group). In Part 2, there were two discontinuations; one was discontinued due to an AE and the other did not to return during follow-up, but provided no explanation (both were in the placebo group).

Efficacy

After eight weeks of BID dosing in Part 1, patients treated with *trabodenoson* co-administered with *latanoprost* experienced further mean reductions of IOP of 3.4 and 4.9 mmHg from diurnal and study baselines, respectively, beyond the IOP-lowering of *latanoprost*. After switching to QD *trabodenoson* in Part 2, and treating for an additional four weeks, QD dosing with *trabodenoson* resulted in a mean reduction in IOP of 4.3 and 5.8 mmHg from diurnal and study baseline, respectively, from the IOP on *latanoprost* alone. At the end of Part 2 (after 12 weeks), the IOP-lowering seen in the Study Eye (the eye treated with *trabodenoson)* was statistically significantly greater than the IOP drop of the patient's Control Eye (the patient's other eye that only received QD *latanoprost*).

In Part 1 the IOP drop at the end of 8 weeks of treatment, in this population of *latanoprost* poor-responders, was less than *timolol* BID (0.5%) which dropped pressure 6.1 and 7.6 mmHg, on average from diurnal and study baselines, respectively.

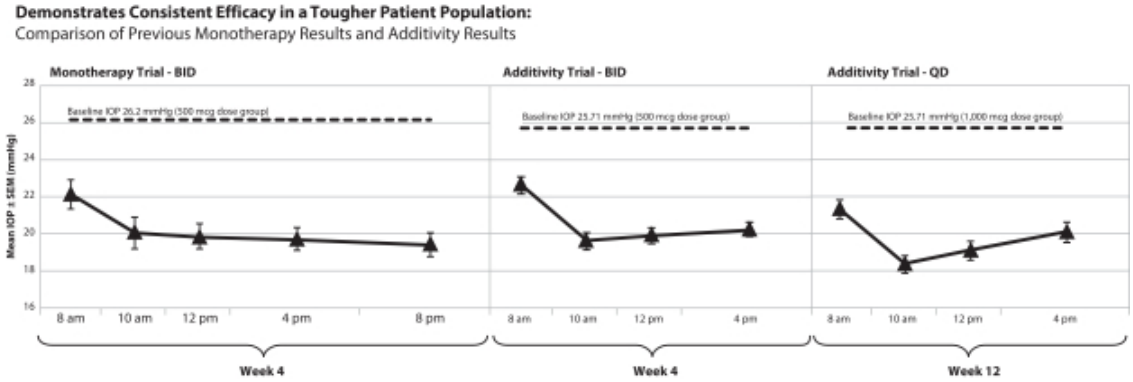


In Part 2 of the trial, QD *trabodenoson* lowered IOP an additional 4.3 and 5.8 mmHg from diurnal and study baseline, respectively, beyond the effect of *latanoprost* alone in this population of *latanoprost* poor-responders.

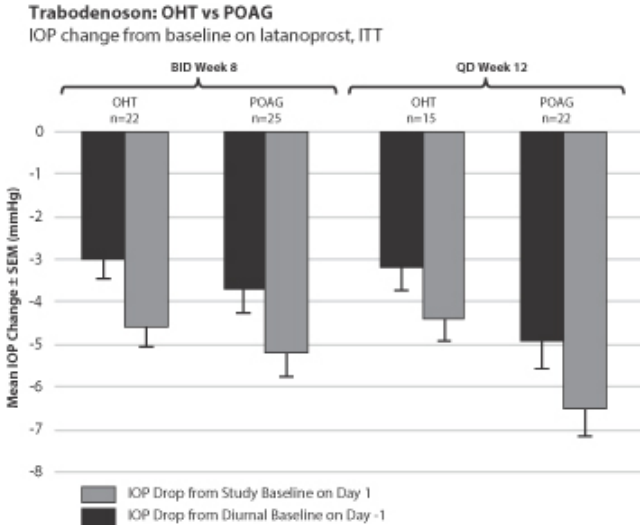
Consistency of Results across Phase II Studies

Mean reductions in IOP from study baseline ranging from 5.0 mmHg after four weeks of BID treatment to 5.8 mmHg after four weeks of QD treatment in the trial were similar to the 6.5 mmHg IOP reduction seen at the end of the four week *Trabodenoson Phase 2 Tolerability, Safety and Efficacy of Monotherapy in Glaucoma Patients* trial (the monotherapy trial). In the monotherapy trial, patients received only *trabodenoson*. The patients in the 2014 additivity trial represented a different patient

population than those studied in the monotherapy trial. These patients had inadequate responses to *latanoprost,* as evidenced by persistently high IOP, despite *latanoprost* treatment for four weeks prior to randomization. This patient population typically requires the addition of a second drug to their PGA therapy to further lower IOP. Patients in the monotherapy trial, by contrast, were removed from all glaucoma medications, and thus represented a typical patient population studied in a Phase 3 glaucoma trial. Despite these differences in the patient populations, the efficacy of *trabodenoson* was consistent across trials, suggesting that *trabodenoson*'s mechanism of action is effective across a wide-range of glaucoma disease severity.



Both OHT and POAG patients responded to *trabodenoson* with POAG subjects showing the largest IOP drops.



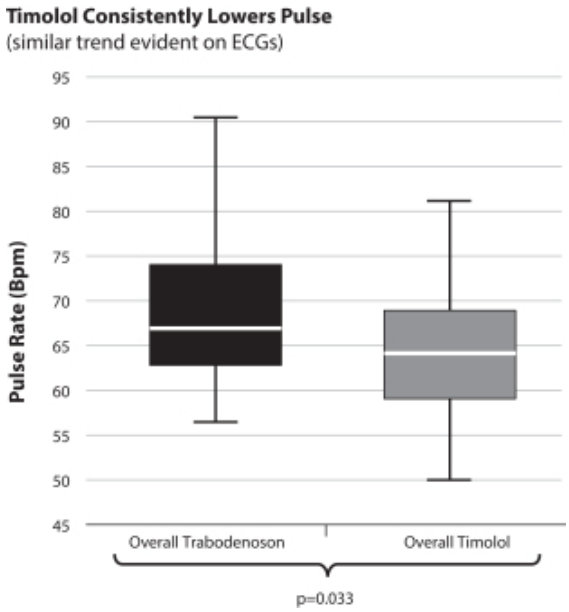
Safety and Tolerability

With the exception of a single patient who received placebo plus *latanoprost*, no patients dropped out of the trial as a result of a drug-related adverse effect or due to drug intolerability. *Trabodenoson* was well tolerated in the eye, with no drug related hyperemia detectable by ocular exam at four, eight or 12 weeks. Mild hyperemia seen on the first day of dosing in a minority of patients was back to baseline by the 1 week post dose ocular exams. *Trabodenoson* had no detectable systemic effects in any of the non-ocular

examinations, ECG evaluations or laboratory tests performed. Overall adverse events were similar in the BID phase (*Trabodenoson* 36%; *Timolol* 29%), with the *trabodenoson* rate dropping to 26% without the first-day hyperemias, and were also similar in the QD phase (*Trabodenoson* 16%; Placebo 14%) between treatment groups. However, *timolol* (dosed in one eye only) had systemic adverse events associated with systemic beta blockade, including: dizziness, headache, fatigue and symptomatic sinus bradycardia.

Patients randomized to *timolol* also had lower pulse rates than in the *trabodenoson* group (the pulse rate was measured 30 minutes and one hour after dosing). This difference was statistically significant in the overall data (p=0.033) as well as at the individual timepoints (p=0.041 and p=0.030 at the 30 minute and one hour post-dose timepoints, respectively).

The pulse rates for both groups are shown in the boxplot below, which includes the minimum and maximum values, median (white line), and the boundaries of the upper and lower quartiles (top and bottom of the box).



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*.

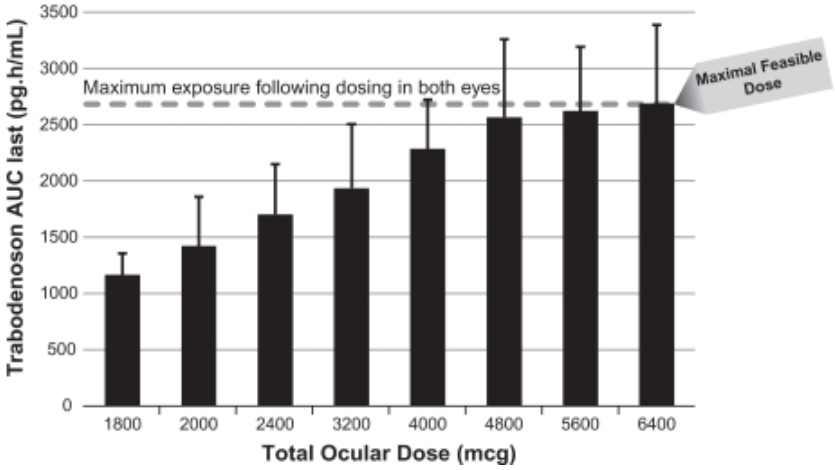
Early Terminations and Withdrawals

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.

The Amount of Trabodenoson Entering the Body Reaches a Plateau, Limiting Systemic Effects



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.

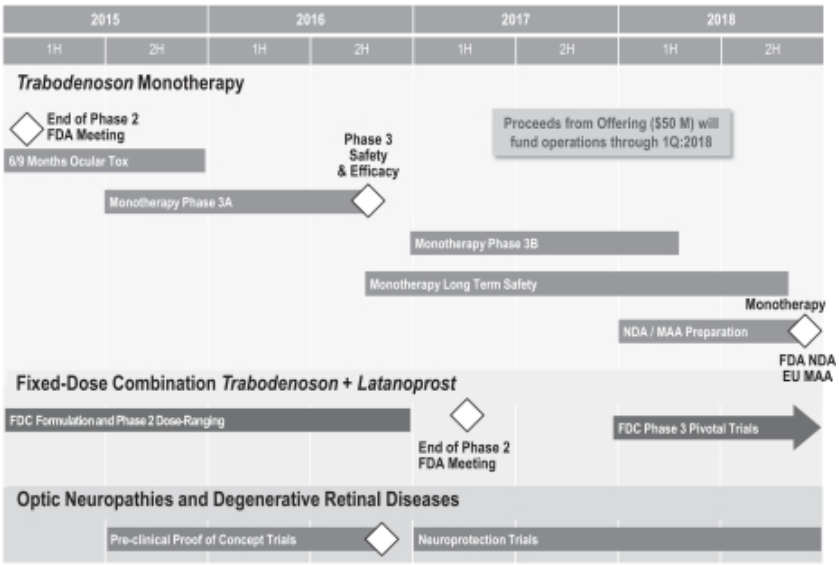
Efficacy (IOP-lowering), tolerability, safety and pharmacokinetics assessments were performed following study drug administration, and dose escalation from one cohort to the next cohort proceeded only after masked review of the safety data from the preceding cohort.

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

Having completed our Phase 2 trials and End-of-Phase 2 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 neuropathy. The figure below shows our plans for upcoming clinical trials.



Trabodenoson

We had 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. At the meeting, we reached agreement on the design of our initial Phase 3 study, as well as the overall regulatory path for trabodenoson. We plan to start our Phase 3 program for trabodenoson monotherapy in the fourth quarter of 2015, when the manufacturing (in accordance with the current Good Manufacturing Practice, or cGMP), packaging and labeling of the study drug are complete. We expect to report top-line data from the first pivotal trial in the program by late 2016. If the primary objectives of all of the trials in the Phase 3 program are met, we plan to submit an NDA.

The overall program will encompass a total subject exposure to trabodenoson of at least 1,300 patients. The final design of the second Phase 3 trial will be impacted by the findings of the initial Phase 3 trial. Following a run-in period, both trials are expected to run for at least 12 weeks of active treatment with the primary endpoint of IOP-lowering over the day.

The initial Phase 3 trial will be a three-month study with five treatment arms, for a total of approximately 400 patients. There will be 3 trabodenoson treatment arms. The *trabodenoson* doses to be evaluated are 1,000 mcg QD, 2,000 mcg QD, and 1,500 mcg BID. The trial will investigate both once-daily (QD) and twice-daily (BID) dosing, as some patients may benefit from a twice daily dosing regimen. The primary efficacy endpoint of the study is IOP, measured at four time points during the day after 4, 6 and 12 weeks of treatment. The IOP of the trabodenoson treated subjects will be statistically compared to those of placebo treated subjects. A timolol arm will be included for study validation, but not for statistical comparison.

The FDA requires that a total of at least 1,300 patients be 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 are expected to begin in late 2016. If the enrollment projections are met, the first data from our Phase 3 program is anticipated in late 2016. We are planning to complete the long-term safety study in late 2018. If the primary objectives of all trials in 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 *trabodenoson* as a monotherapy.

The results of the Phase 2 trial that evaluated the efficacy and safety of the combination of *latanoprost* and *trabodenoson*, at two dose levels, and when given QD and BID, will inform the design and 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 FDC clinical supplies are available, based on discussion at our End-of-Phase 2 meeting with the FDA we believe that the FDA will allow us to continue the Phase 2 development using several FDC formulations with various dose combinations. 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 early 2018. 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 and Degenerative Retinal Diseases

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 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. We also plan to start pre-clinical and proof-of-concept trials for optic neuropathies and degenerative retinal diseases beginning in the second half of 2015.

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 is scheduled to expire in 2031 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 Parts 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 therapeutics 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 U.S. 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, as applicable, which may include the Federal Anti-Kickback Statute, the Federal False Claims Act, as amended, the privacy and security 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 or entity, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully, directly or indirectly, in cash or in kind, 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.

Federal false claims and false statement laws, including the civil False Claims Act, prohibits any person or entity 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 civil False Claims Act in connection with their off-label promotion of drugs. Penalties for a civil 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 civil False Claims Act and certain states have enacted laws modeled after the Federal False Claims Act.

Additionally, HIPAA created additional federal criminal statutes that prohibit, among other things, 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 under the Physician Payments Sunshine Act, 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, as well as certain ownership and investment interests held by physicians and their immediate family members. 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 on certain types of individuals and organizations. 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, certain state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other and from HIPAA 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 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.

By way of example, 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 U.S. 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 requires certain pharmaceutical manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exception, 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 CMS 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 was made 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 improve quality of care and lower program costs of Medicare, Medicaid and the Children's Health Insurance Program, 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. For example, 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 2012 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 eleven full-time employees as of July 31, 2015. 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 3,500 square feet of leased office space under a lease that expires on September 30, 2015. In May 2015, we signed a lease for approximately 11,000 square feet for our new corporate headquarters in Lexington, Massachusetts. We expect to occupy this space in September 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	54	President, Chief Executive Officer and Director
Rudolf Baumgartner, M.D.	56	Executive Vice President and Chief Medical Officer
William K. McVicar, Ph.D.	57	Executive Vice President and Chief Scientific Officer
Dale Ritter	64	Vice President—Finance
Non-Management Directors:		
Ittai Harel(1)(2)(3)	47	Director
Paul G Howes	60	Director
A.N. “Jerry” Karabelas, Ph.D.	62	Director
Isai Peimer(1)(2)(3)	37	Director
Richard N. Spivey, PharmD, PhD(3)	63	Director
Martin Vogelbaum(1)(2)	52	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 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, Johns Hopkins University and the National Institutes of Health.

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 College 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 and Principal Financial and Accounting Officer, Treasurer and Secretary since

August 2014. From May 2011 to November 2013, Mr. Ritter served in various roles at Coronado Biosciences, Inc., most recently as Senior Vice President, Finance and Chief Accounting Officer. From January 2011 to May 2011, Mr. Ritter served as an Independent Financial Consultant and from 1994 to 2009 Mr. Ritter served in various roles and most recently as Senior Vice President and Chief Accounting Officer at Indevus Pharmaceuticals, Inc. 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., Medisafe Project, Ltd. and EarlySense Ltd., also serving as Chairman of the boards of directors of Lifebond Ltd. and EarlySense Ltd. Additionally, Mr. Harel serves on the Compensation Committees 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 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, which is now owned by Valeant Pharmaceuticals International, Inc., from July 2003 to February 2007. Prior to this time, Mr. Howes served in a variety of senior roles at Merck & Co., Inc. for sixteen years. 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 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.

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 Chairperson 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 the founder and 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 and since May 2015 has served as a member of the board of REGENEXBIO Inc. 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 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 Managing Director 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 include his experience on numerous committees of boards of directors of pharmaceutical companies and his work in advising developing life sciences companies.

Richard N. Spivey, PharmD, PhD has served as one of our directors since July 2015. Dr. Spivey currently serves as a scientific advisor to the pharmaceutical industry and as a member of the Board of Councilors, University of Southern California, and School of Pharmacy. From 2010 to 2015, he was the Senior Vice President, Global Regulatory Affairs at Allergan, plc. From 2002 to 2010, Dr. Spivey served various roles at Meda AB (previously MedPointe Inc.), most recently as the Chief Scientific Officer (Head of R&D). Dr. Spivey has also held positions at Pharmacia Corporation (now Pfizer Inc.), Schering-Plough Corporation (now Merck & Co.), Parke-Davis Pharmaceutical Research Division, and Boots Pharmaceuticals, Inc. Dr. Spivey received his PharmD from the University of Southern California and his PhD from the College of Pharmacy, University of Minnesota. We believe that Dr. Spivey's qualifications to sit on our Board include his distinguished background in drug development and regulatory affairs spanning thirty-years of experience working at leading pharmaceutical 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 through the present date, and NephroGenex, Inc., where he served as director from October 2013 to May 2014. 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 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 Our nominating and governance committee and Board of Directors may 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 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. The composition and functioning of our Board of Directors and each of our committees complies 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, our Board of Directors is 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. The following persons have been designated to serve as directors in the following classes until the term specified below or until his earlier death, resignation or removal:

- Our Class I directors are David P. Southwell and Richard N. Spivey, PharmD, PhD (term expires on date of annual meeting of stockholders following the year ending December 31, 2017);
- Our Class II directors are Isai Peimer, Martin Vogelbaum and Ittai Harel (term expires on date of annual meeting of stockholders following the year ending December 31, 2015); and
- Our Class III directors are Paul G. Howes and A.N. “Jerry” Karabelas, Ph.D. (term expires on date of annual meeting of stockholders following the year ending December 31, 2016).

Our amended and restated certificate of incorporation and amended and restated bylaws 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 Chairperson 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 Chairperson 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 Chairperson, 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 do not require our Chairperson 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

Isai Peimer, Ittai Harel and Martin Vogelbaum currently serve on the audit committee, which is chaired by Isai Peimer. 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 Isai Peimer 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, retention and treatment of complaints received regarding ethics-related issues or potential violations of our code of business conduct and ethics and accounting and auditing-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

Martin Vogelbaum, Isai Peimer and Ittai Harel currently serve on the compensation committee, which is chaired by Martin Vogelbaum. 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

Ittai Harel, Richard N. Spivey, PharmD, PhD and Isai Peimer currently serve on the nominating and corporate governance committee, which is chaired Ittai Harel. 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

Our Board of Directors has adopted 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. A current copy of the code is 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.

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 and other documents incorporated by reference herein.

All share and pre-share figures in this section have been adjusted to reflect a 1-for-3.39 and 1-for-1.197 reverse stock splits of our common stock and a proportional adjustment to the existing conversion ratio for each series of our redeemable convertible preferred stock, which became effective on November 26, 2014 and January 21, 2015, respectively.

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 former 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, 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 Managing Director at 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 were exercised in full during 2014.

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 former 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, of which Rho Ventures IV, L.P, Rho Ventures IV (QP), L.P., Rho Ventures IV GmbH & Co. BETEILIGUNGS KG and Rho Ventures IV Holdings LLC are affiliated funds.
(5) Isai Peimer, a member of our Board of Directors, is a Managing Director at MedImmune Ventures, Inc.

Debt Financings

In December 2014, we sold subordinated convertible promissory notes, or the 2014 bridge notes, in the aggregate original principal amount of $2.0 million to existing stockholders. As consideration for our issuance of the 2014 bridge notes, each investor paid us an amount equal to the original principal amount of the note issued to the investor. The 2014 bridge notes mature on June 30, 2015, accrue interest at the rate of 8% per annum and are subordinate to all other senior indebtedness of the Company. As of the date of this prospectus, the aggregate outstanding principal and accrued interest under the 2014 bridge notes is approximately $2.0 million. Upon the closing of our initial public offering, all outstanding principal and accrued interest of the 2014 bridge notes, automatically converted into common stock at the initial public offering price. The following table summarizes the participation in the 2014 bridge notes 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 Subordinated Convertible Promissory Note
Devon Park Bioventures, L.P.(1)	$ 626,942.90
Rho Ventures IV, L.P.(2)	$ 27,797.11
Rho Ventures IV (QP), L.P.(2)	$ 146,910.56
Rho Ventures IV GmbH & Co. Beteiligungs KG(2)	$ 153,102.29
Rho Ventures IV Holdings LLC(2)	$ 104,780.66
Care Capital Investments III, LP(3)	$ 369,989.00
Care Capital Offshore Investments III, LP(3)	$ 6,178.93
MedImmune Ventures, Inc.(4)	$ 338,551.12
Pitango Venture Capital Fund IV, L.P.(5)	$ 220,975.53
Pitango Venture Capital Principals Fund IV, L.P.(5)	$ 4,771.90

(1) Devang V. Kantesaria, a former 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) Martin Vogelbaum, a member of our Board of Directors, is a Partner at Rho, of which the Rho Venture Entities 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 the Care Capital Entities are affiliated funds.
(4) Isai Peimer, a member of our Board of Directors, is a Managing Director at MedImmune Ventures, Inc.
(5) Ittai Harel, a member of our Board of Directors, is a general partner with Pitango Venture Capital, of which the Pitango Venture Capital Fund Entities are affiliated funds.

Agreements With Our Stockholders

In connection with our preferred stock financings, we entered into a third amended and restated investor rights agreement, or Investor Rights Agreement, and a third amended and restated stockholders agreement, as amended, or 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.

The rights under each of the Investor Rights Agreement and the Stockholders Agreement terminated upon the closing of our initial public offering, other than certain registration rights for certain holders of our preferred stock described below under “Description of Capital Stock.”

Indemnification Agreements

Our Seventh 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

The audit committee of our Board of Directors has 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 provides 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 August 7, 2015, 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 (i) 16,327,003 shares of common stock outstanding as of June 30, 2015, and (ii) 3,863,391 shares of common stock issued pursuant to conversion of the $21,000,000 principal amount of the 2020 Convertible Notes through August 7, 2015 which includes 3,333,319 shares related to the underlying 2020 Convertible Notes and 530,072 shares issued pursuant to the interest make-whole provision, which the Company elected to settle in shares; and excludes (i) 1,394,075 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2015, at a weighted-average exercise price of $4.92 per share; and (ii) 56,408 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2015, which have an exercise price of $6.204 per share. Shares of common stock that may be acquired by an individual or group within 60 days of June 30, 2015, 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 to Purchase Additional Shares)" is based on 25,590,394 shares of our common stock outstanding after this offering, including the 5,400,000 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 to Purchase Additional Shares)" is based on 26,400,394 shares of our common stock outstanding after this offering, including the 5,400,000 shares of our common stock that we are selling in this offering and assumes the exercise in full of the underwriters' option to purchase 810,000 additional shares.

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	Percentage of Shares Beneficially Owned Prior to this Offering	After this Offering (No Exercise of the Underwriters' Option to Purchase Additional Shares)	After this Offering (Full Exercise of the Underwriters' Option to Purchase Additional Shares)
5% Stockholders				
Devon Park Associates Entities(1)	3,253,566	16.1%	12.7%	12.3%
Rho Ventures Entities(2)	2,870,584	14.2%	11.2%	10.9%
Care Capital Entities(3)	2,277,139	11.3%	8.9%	8.6%
MedImmune Ventures, Inc.(4)	1,917,906	9.5%	7.5%	7.3%
Pitango Venture Capital Fund Entities(5)	1,292,584	6.4%	5.1%	4.9%
Named executive officers and directors				
David P. Southwell(6)	99,624	*	*	*
Rudolf Baumgartner, M.D.(7)	177,821	*	*	*
William K. McVicar, Ph.D.(8)	157,978	*	*	*
Dale Ritter(9)	10,995	*	*	*
Ittai Harel(10)	9,857	*	*	*
Paul G Howes(11)	117,506	*	*	*
A.N. "Jerry" Karabelas, Ph.D.(12)	2,286,996	11.3%	8.9%	8.7%
Isai Peimer(13)	1,927,763	9.5%	7.5%	7.3%
Richard N. Spivey, Pharm.D., Ph.D.	–	*	*	*
Martin Vogelbaum(14)	9,857	*	*	*
All directors and executive officers as a group (10 persons) (15)	4,798,397	23.5%	18.6%	18.0%

* Represents beneficial ownership of less than one percent.

(1) Consists of (a) 3,243,709 shares beneficially owned by Devon Park Bioventures, L.P. and (b) 9,857 shares of common stock issuable upon the exercise of options exercisable within 60 days after June 30, 2015 beneficially owned by Devon Park Associates, 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, 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 Associates Entities as described above. The address for Devon Park Associates Entities is 1400 Liberty Ridge Drive, Suite 103, Wayne, Pennsylvania, 19087.

(2) Consists of (a) 892,415 shares beneficially owned by Rho Ventures IV (QP), L.P. ("Rho QP"), (b) 930,029 shares beneficially owned by Rho Ventures IV GmbH & Co. BETEILIGUNGS KG ("Rho GmbH"), (c) 751,579 shares beneficially owned by Rho Ventures IV Holdings LLC ("Rho Holdings"), (d) 168,850 shares beneficially owned by Rho Ventures IV, L.P. ("Rho IV") and (e) 127,711 shares beneficially owned by Rho Ventures IV-A, L.P. ("Rho IV-A"). 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 or managing member, 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. The address for the Rho Venture Entities is 152 West 57th Street, 23rd Floor, New York, New York 10019.

(3) Consists of (a) 713,077 shares beneficially owned by Care Capital Investments II, LP. ("Investments II"), (b) 1,490,240 shares beneficially owned by Care Capital Investments III, L.P ("Investments III"), (c) 48,938 shares beneficially owned by Care Capital Offshore Investments II, L.P. ("Offshore II") and (d) 24,884 shares beneficially owned by Care Capital Offshore Investments III, LP. ("Offshore III") 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 1,917,906 shares beneficially owned by MedImmune Ventures, Inc. The voting and investment power of the shares held by MedImmune Ventures, Inc. is determined by Ron Laufer, Senior Managing Director of MedImmune Ventures, Inc. Isai Peimer, a member of our Board of Directors, is a Managing Director at MedImmune Ventures, Inc. The address of MedImmune Ventures, Inc. is 1 MedImmune Way, Gaithersburg, Maryland 20878.

(5) Consists of (a) 1,265,276 shares beneficially owned by Pitango Venture Capital Fund IV L.P. ("Pitango Fund IV") and 27,308 shares beneficially owned by Pitango Venture Capital Fund Principals IV L.P. ("Pitango Principals"). 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) Includes 99,624 shares of common stock issuable upon the exercise of options exercisable within 60 days after June 30, 2015.

(7) Includes 52,179 shares of common stock issuable upon the exercise of options exercisable within 60 days after June 30, 2015.

(8) Consists of 51,658 shares of common stock issuable upon the exercise of options exercisable within 60 days after June 30, 2015.

(9) Includes 10,995 shares of common stock issuable upon the exercise of options exercisable within 60 days after June 30, 2015.

(10) Consists of 9,857 shares of common stock issuable upon the exercise of options exercisable within 60 days after June 30, 2015.

(11) Includes 16,017 shares of common stock issuable upon the exercise of options exercisable within 60 days after June 30, 2015.

(12) In addition to the shares described in note (3) above, includes 9,857 shares of common stock issuable upon the exercise of options exercisable within 60 days after June 30, 2015.

(13) In addition to the shares described in note (4) above, includes 9,857 shares of common stock issuable upon the exercise of options exercisable within 60 days after June 30, 2015.

(14) Consists of 9,857 shares of common stock issuable upon the exercise of options exercisable within 60 days after June 30, 2015.

(15) Includes 269,901 shares of common stock issuable upon the exercise of options exercisable within 60 days after June 30, 2015.

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. 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

Our authorized capital stock consists of 120,000,000 shares of common stock, par value $0.01 per share, and 5,000,000 shares of preferred stock, par value $0.001 per share, all of which shares of preferred stock are undesignated.

As of June 30, 2015, 16,327,003 shares of our common stock were outstanding and held by 52 stockholders of record. In addition, as of June 30, 2015, no shares of preferred stock were outstanding. Further, as of June 30, 2015, we had outstanding options to purchase 1,394,075 shares of our common stock, at a weighted average exercise price of $4.92 per share, 70,100 of which are vested and exercisable.

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

Our Board of Directors currently has the authority, without further action by our stockholders, to issue up to 5,000,000 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. No shares of preferred stock are outstanding, and we have no present plans to issue any shares of preferred stock.

Our warrants are exercisable for 56,408 shares of our common stock at $6.204 per share rather than Series AA Preferred Stock after the effect of our 1-for-3.39 and 1-for-1.197 reverse stock splits. 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. 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.

Registration Rights

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

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 90 days after the closing of this offering.

Form S-3 Registration Rights

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

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 our initial public offering, or February 23, 2020.

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

Our certificate of incorporation and bylaws 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 5,000,000 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

We are 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

Our common stock is listed on The NASDAQ Global Market under the trading symbol “ITEK.”

Transfer Agent and Registrar

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

SHARES ELIGIBLE FOR FUTURE SALE

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.

Upon the closing of this offering of common stock, 25,590,394 shares of our common stock will be outstanding, assuming no exercise of the underwriters' option to purchase additional shares and no exercise of outstanding options, including (i) 16,327,003 shares of common stock issued and outstanding as of June 30, 2015, (ii) 3,863,391 shares of common stock issued pursuant to the conversion of $21,000,000 principal amount of the 2020 Convertible Notes, which includes 3,333,319 shares related to the underlying 2020 Convertible Notes and 530,072 shares issued pursuant to the interest make-whole provision, which the Company elected to settle in shares, and (iii) 5,400,000 shares of our common stock that we are selling in this offering. 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 256,000 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 August 7, 2015; or
- the average weekly trading volume of our common stock on the NASDAQ Global Market 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 executive officers, directors and such directors' affiliates, who collectively held approximately 8.7 million shares of common stock as of June 30, 2015, 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 90 days from the date of this prospectus prepared for this offering without the prior written consent of each of Cowen and Company, LLC, Piper Jaffray & Co. and Nomura Securities International, Inc., 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 90-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

The holders of approximately 8.8 million shares of common stock or their transferees are 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 have filed a Form S-8 registration statement under the Securities Act to register shares of our common stock subject to options outstanding or reserved for issuance under our stock plans. Shares covered by this registration statement will thereupon be eligible for sale in the public markets, subject to Rule 144 limitations applicable to affiliates and any lock-up agreements. For a more complete discussion of our stock plans, see "Equity—2014 Stock Option and Incentive Plan", "Equity—2004 Stock Option and Incentive Plan" and "Equity—Employee Stock Purchase Plan" from our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2015 incorporated herein.

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 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 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, estate 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

Subject to the discussion below under "Withholding and Information Reporting Requirements—FATCA,", a non-U.S. holder generally 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.

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 currently applies to payments of dividends on our common stock, 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, Piper Jaffray & Co. and Nomura Securities International, Inc. are the representatives of the underwriters.

Underwriter	Number of Shares
Cowen and Company, LLC	2,349,000
Piper Jaffray & Co.	2,079,000
Nomura Securities International, Inc.	972,000
Total	5,400,000

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 option to purchase additional shares 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.

Option to Purchase Additional Shares

We have granted to the underwriters an option to purchase up to 810,000 additional shares of common stock at the public offering price, less the underwriting discount, in this offering of common stock. This option is exercisable for a period of 30 days. 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.

We estimate that the total expenses of this offering of common stock, excluding underwriting discounts and commissions, will be approximately $500,000 and are payable by us. We have also agreed to reimburse the underwriters for certain of their expenses as set forth in the underwriting

agreement, including legal fees incurred in the qualification of this offering and the concurrent offering of notes with the Financial Regulatory Authority, or FINRA, in an amount of up to $25,000, which amount is deemed to be underwriting compensation by FINRA.

		Total	
	Per Share	Without Overallotment	With Overallotment
Public offering price	$ 12.75	$68,850,000	$79,177,500
Underwriting discounts and commissions	$ 0.765	$ 4,131,000	$ 4,750,650
Proceeds, before expenses, to Inotek	$ 11.985	$64,719,000	$74,426,850

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 $0.459 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. Sales of shares of common stock may be made by affiliates of certain of the underwriters.

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

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.

Our common stock is listed on The NASDAQ Global Market under the symbol “ITEK”.

Price Stabilization, Short Positions and Penalty Bids

In connection with this offering of common stock, 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 option to purchase additional shares. In a naked short position, the number of shares involved is greater than the number of shares in the option to purchase additional shares. The underwriters may close out any short position by exercising their option to purchase additional shares 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 option to purchase additional shares. If the underwriters sell more shares than could be covered by exercise of the option to purchase additional shares 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 and directors and such directors’ affiliates, 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, Piper Jaffray & Co. and Nomura Securities International, Inc., for a period of 90 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 such directors’ affiliates 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 this 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 10b5-1(c) under the Exchange Act, provided that no sale or other disposition under such trading plan may occur during the 90-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; and (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 other documents incorporated by reference herein. 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, Piper Jaffray & Co. and Nomura Securities International, Inc., 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, Piper Jaffray & Co. and Nomura Securities International, Inc. 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.

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. In addition, the underwriters of this offering of common stock are also the underwriters for the concurrent offering of notes.

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.

Israel

In the State of Israel this prospectus shall not be regarded as an offer to the public to purchase shares of common stock under the Israeli Securities Law, 5728 – 1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728–1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions (the "Addressed Investors"); or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728 – 1968, subject to certain conditions (the "Qualified Investors"). The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. The company has not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728 – 1968. We have not and will not distribute this prospectus or make, distribute or direct an offer to subscribe for our common stock to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728 – 1968. In particular, we may request, as a condition to be offered common stock, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728 – 1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728 – 1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728 – 1968 and the regulations promulgated thereunder in connection with the offer to be issued common stock; (iv) that the shares of common stock that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728 – 1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728 – 1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor's name, address and passport number or Israeli identification number.

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.

Notice to Prospective Investors in Hong Kong

The contents of this document have not been reviewed or approved by any regulatory authority in Hong Kong. This document does not constitute an offer or invitation to the public in Hong Kong to acquire shares. Accordingly, unless permitted by the securities laws of Hong Kong, no person may

issue or have in its possession for the purposes of issue, this document or any advertisement, invitation or document relating to the shares, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong other than in relation to shares which are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" (as such term is defined in the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) ("SFO") and the subsidiary legislation made thereunder); or in circumstances which do not result in this document being a "prospectus" as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32, Laws of Hong Kong) ("CO"); or which do not constitute an offer or an invitation to the public for the purposes of the SFO or the CO. The offer of the shares is personal to the person to whom this document has been delivered, and a subscription for shares will only be accepted from such person. No person to whom a copy of this document is issued may issue, circulate or distribute this document in Hong Kong, or make or give a copy of this document to any other person. You are advised to exercise caution in relation to the offer. If you are in any doubt about any of the contents of this document, you should obtain independent professional advice.

Notice to Prospective Investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor pursuant to Section 274 of the Securities and Futures Act, Chapter 289 of Singapore ("SFA"), (ii) to a relevant person (as defined in Section 275(2) of the SFA), or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased pursuant to an offer made in reliance on Section 275 of the SFA by a relevant person which is:

(a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

(b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor,

shares, debentures and units of shares, and debentures of that corporation, or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferable for six months after that corporation or that trust has acquired the shares under Section 275 except:

(1) to an institutional investor or to a relevant person (as defined in Section 275(2) of the SFA), or any person pursuant to Section 275(1A) of the SFA (in the case of that corporation) or Section 276(4)(i)(B) of the SFA (in the case of that trust);

(2) where no consideration is or will be given for the transfer; or

(3) where the transfer is by operation of law.

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 financial statements of Inotek Pharmaceuticals Corporation incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2014, have been audited by McGladrey LLP, an independent registered public accounting firm, as stated in their report incorporated by reference herein, and have been so incorporated 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 333-206027) 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 the exhibits to the reports or other documents incorporated by reference herein. 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.

We are subject to the informational requirements of the Exchange Act and, as a result, we 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.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The following documents filed by us with the SEC are incorporated by reference into this prospectus. You should carefully read and consider all of these documents before making an investment decision:

- Our Current Report on Form 8-K filed on July 23, 2015;
- Our Current Report on Form 8-K filed on July 21, 2015;
- Our Current Report on Form 8-K filed on June 26, 2015;
- Our Quarterly Report on Form 10-Q for the quarter ended June 30, 2015 filed with the SEC on August 6, 2015;
- Our Current Report on Form 8-K filed on June 2, 2015;
- Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2015 filed with the SEC on May 14, 2015;
- Our Notice and Proxy Statement on Schedule 14A filed on April 29, 2015;
- Our Current Report on Form 8-K filed on April 28, 2015;
- Our Current Report on Form 8-K filed on April 8, 2015;
- Our Annual Report on Form 10-K for the year ended December 31, 2014 filed with the SEC on March 31, 2015;

- Our Current Report on Form 8-K filed on February 26, 2015; and
- The description of our common stock contained in our registration statement on Form 8-A filed with the SEC on February 2, 2015, including any amendments or reports filed for the purpose of updating such description.

Nothing in this prospectus shall be deemed to incorporate information deemed furnished but not filed with the SEC. Any statement contained in a document that is incorporated by reference will be modified or superseded for all purposes to the extent that a statement contained in this prospectus modifies or is contrary to that previous statement. Any statement so modified or superseded will not be deemed a part of this prospectus except as so modified or superseded.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, a copy of any or all of the reports or documents that have been incorporated by reference into this prospectus but not delivered with this prospectus. We will provide these reports upon written or oral request at no cost to the requester. Please direct your request, either in writing or by telephone, to Vice President – Finance, 131 Hartwell Avenue, Suite 105, Lexington, Massachusetts, telephone number (781) 676-2100. In addition, copies of the documents incorporated herein by reference may be accessed at our website at www.inotekpharma.com. The reference to our website address does not constitute incorporation by reference of the information contained on our website, and you should not consider the contents of our website in making an investment decision with respect to our common stock.

Table of Contents

5,400,000 Shares

Common Stock

PROSPECTUS

Cowen and Company **Piper Jaffray** **Nomura**

August 12, 2015