

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

**Form 10-Q**

**QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended March 31, 2017

OR

**TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from \_\_\_\_\_ to \_\_\_\_\_

Commission file number: 001-36829

**Inotek Pharmaceuticals Corporation**

(Exact name of registrant as specified in its charter)

**Delaware**  
(State or other jurisdiction of  
incorporation or organization)

**04-3475813**  
(I.R.S. Employer  
Identification No.)

**91 Hartwell Avenue**  
**Lexington, MA 02421**  
(Address of principal executive office) (Zip Code)

**Registrant's telephone number, including area code:**  
**(781) 676-2100**

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes  No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes  No

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

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input checked="" type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	(Do not check if a smaller reporting company)	
Emerging growth company	<input checked="" type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes  No

As of May 9, 2017, there were 26,986,318 shares of common stock, \$0.01 par value per share, outstanding.

## FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements that involve risks and uncertainties, as well as assumptions that, if they never materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this Quarterly Report on Form 10-Q are forward-looking statements. In some cases, you can identify forward-looking statements by words such as “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would,” or the negative of these words or other comparable terminology. These forward-looking statements 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 U.S. Food and Drug Administration (the “FDA”);
- the success, timing and cost of our current Phase 3 program for *trabodenson* as a monotherapy and planned Phase 3 and other clinical trials and Phase 2 clinical trial for our fixed-dose combination 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 potential 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 safety, tolerability and 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 a potential commercial launch of our product candidates and potential future sales of our current product candidates or any other potential products if any are approved for marketing;
- our expectations regarding licensing, acquisitions and strategic operations;
- the potential advantages of our product candidates;
- 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 Quarterly Report on Form 10-Q.

Any forward-looking statements in this Quarterly Report on Form 10-Q reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under Part II, Item 1A. Risk Factors in this Quarterly Report on Form 10-Q and elsewhere in this Quarterly Report on Form 10-Q. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Quarterly Report on Form 10-Q also contains estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

Inotek Pharmaceuticals Corporation

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## PART I — FINANCIAL INFORMATION

## Item 1. Consolidated Financial Statements

**Inotek Pharmaceuticals Corporation**  
**Consolidated Balance Sheets**  
**(Unaudited)**  
**(In thousands, except share and per share amounts)**

	March 31, 2017	December 31, 2016
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 25,273	\$ 29,798
Short-term investments	89,432	96,675
Prepaid expenses and other current assets	1,928	1,876
Total current assets	116,633	128,349
Property and equipment, net	1,122	1,130
Other assets	168	168
Total assets	<u>\$ 117,923</u>	<u>\$ 129,647</u>
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 1,902	\$ 1,592
Accrued expenses and other current liabilities	2,886	4,416
Accrued interest	480	1,204
Total current liabilities	5,268	7,212
2021 Convertible Notes, net of issuance costs	49,099	48,960
Other long-term liabilities	292	307
Total liabilities	<u>54,659</u>	<u>56,479</u>
Commitments and Contingencies (Note 7)		
Stockholders' equity:		
Preferred Stock, \$0.001 par value: 5,000,000 shares authorized and no shares issued or outstanding	—	—
Common stock, \$0.01 par value: 120,000,000 shares authorized at March 31, 2017 and December 31, 2016; 26,986,318 shares issued and outstanding at March 31, 2017 and December 31, 2016	270	270
Additional paid-in capital	312,613	311,829
Accumulated deficit	(249,547)	(238,877)
Accumulated other comprehensive loss	(72)	(54)
Total stockholders' equity	<u>63,264</u>	<u>73,168</u>
Total liabilities and stockholders' equity	<u>\$ 117,923</u>	<u>\$ 129,647</u>

*The accompanying notes are an integral part of these consolidated financial statements.*

**Inotek Pharmaceuticals Corporation**  
**Consolidated Statements of Operations**  
**(Unaudited)**  
**(In thousands, except share and per share amounts)**

	Three Months Ended March 31,	
	2017	2016
Operating expenses:		
Research and development	\$ (7,097)	\$ (7,615)
General and administrative	(2,869)	(2,522)
Loss from operations	(9,966)	(10,137)
Interest expense	(876)	—
Interest income	172	69
Net loss	<u>\$ (10,670)</u>	<u>\$ (10,068)</u>
Net loss per share attributable to common stockholders—basic and diluted	<u>\$ (0.40)</u>	<u>\$ (0.38)</u>
Weighted-average number of shares outstanding—basic and diluted	<u>26,986,318</u>	<u>26,423,394</u>

*The accompanying notes are an integral part of these consolidated financial statements.*

Inotek Pharmaceuticals Corporation

Consolidated Statements of Comprehensive Loss  
(Unaudited)  
(In thousands)

	Three Months Ended March 31,	
	2017	2016
Net loss	\$ (10,670)	\$ (10,068)
Other comprehensive income:		
Net unrealized income (loss) on marketable securities	(18)	11
Total comprehensive loss	<u>\$ (10,688)</u>	<u>\$ (10,057)</u>

*The accompanying notes are an integral part of these consolidated financial statements.*

**Inotek Pharmaceuticals Corporation**

**Consolidated Statements of Cash Flows**  
**(Unaudited)**  
**(In thousands)**

	<b>Three Months Ended March 31,</b>	
	<b>2017</b>	<b>2016</b>
<b>Cash flows from operating activities:</b>		
Net loss	\$ (10,670)	\$ (10,068)
<b>Adjustments to reconcile net loss to cash used in operating activities:</b>		
Noncash interest expense	139	—
Noncash rent expense	(15)	(16)
Amortization of premium on marketable securities	71	43
Depreciation	61	37
Stock-based compensation	784	486
<b>Changes in operating assets and liabilities:</b>		
Prepaid expenses and other assets	(45)	52
Accounts payable	310	(257)
Accrued expenses and other current liabilities	(2,254)	730
Net cash used in operating activities	<u>(11,619)</u>	<u>(8,993)</u>
<b>Cash flows from investing activities:</b>		
Purchases of short-term investments	(12,722)	(24,161)
Proceeds from the maturities of short-term investments	19,869	11,833
Purchases of property and equipment	(53)	(15)
Net cash provided by (used in) investing activities	<u>7,094</u>	<u>(12,343)</u>
<b>Cash flows from financing activities:</b>		
Net cash provided by financing activities	<u>—</u>	<u>—</u>
Net change in cash and cash equivalents	(4,525)	(21,336)
Cash and cash equivalents, beginning of period	29,798	80,042
Cash and cash equivalents, end of period	<u>\$ 25,273</u>	<u>\$ 58,706</u>
<b>Supplemental disclosure of cash flow information:</b>		
Cash paid for interest	<u>\$ 1,462</u>	<u>\$ —</u>
<b>Supplemental disclosure of noncash investing and financing activities:</b>		
Net unrealized gain (loss) on marketable securities	<u>\$ (18)</u>	<u>\$ 11</u>

*The accompanying notes are an integral part of these consolidated financial statements.*

# INOTEK PHARMACEUTICALS CORPORATION

## Notes to Consolidated Financial Statements (Amounts in thousands, except share and per share data)

### 1. Organization and Operations

Inotek Pharmaceuticals Corporation (the “Company”) is a clinical-stage biopharmaceutical company advancing molecules with novel mechanisms of action to address significant diseases of the eye. The Company’s business strategy is to develop and progress its product candidates through human clinical trials. The Company’s headquarters are located in Lexington, Massachusetts.

The Company has devoted substantially all of its efforts to research and development, including clinical trials of its product candidates. The Company has not completed the development of any product candidates. The Company has no current source of revenue to sustain present activities and does not expect to generate revenue until and unless the Company receives regulatory approval of and successfully commercializes its product candidates. The Company is subject to a number of risks and uncertainties similar to those of other life science companies developing new products, including, among others, the risks related to the necessity to obtain adequate additional financing, to successfully develop product candidates, to obtain regulatory approval of products candidates, to comply with government regulations, to successfully commercialize its potential products, to protect proprietary technology and to the dependence on key individuals.

In April 2016, the Company filed a registration statement on Form S-3 containing two prospectuses: (i) a base prospectus which covers the offering, issuance and sale of up to \$200,000 in the aggregate of an indeterminate number of shares of common stock and preferred stock, such indeterminate principal amount of debt securities and such indeterminate number of warrants and units; and (ii) a sales agreement prospectus covering the offering, issuance and sale of up to a maximum aggregate offering price of \$50,000 of the Company’s common stock that may be issued and sold under an at-the-market sales agreement with Cowen and Company, LLC (the “ATM”). The \$50,000 of common stock that may be issued and sold under the ATM reduces the available balance under the base prospectus by the amount issued. The Company did not sell any shares of common stock pursuant to the ATM during the three months ended March 31, 2017. At March 31, 2017, \$45,599 was available for sale of common stock under the ATM. Additionally, in 2016 the Company issued \$52,000 aggregate principal amount of 5.75% Convertible Senior Notes due 2021 pursuant to a Prospectus Supplement to its Form S-3, (the “2021 Convertible Notes”), which further reduces the balance available under the base prospectus to \$98,000 as of March 31, 2017.

As of March 31, 2017, the Company had an accumulated deficit of \$249,547 and \$114,705 of cash and cash equivalents and short-term investments.

The Company will need to expend substantial resources for research and development, including costs associated with the clinical testing of its product candidates and will need to obtain additional financing to fund its operations and to conduct trials for its product candidates. If such products were to receive regulatory approval, the Company would need to prepare for the potential commercialization of its product candidates and fund the commercial launch and continued marketing of its products. The Company expects operating expenses will substantially increase in the future related to additional clinical testing and to support an increased infrastructure to support expanded operations and being a public company.

The Company will require additional funding in the future and may not be able to raise such additional funds. The Company expects losses will continue as it conducts research and development activities. The Company will seek to finance future cash needs through public or private equity offerings, license agreements, debt financings, collaborations, strategic alliances, or any combination thereof. The incurrence of indebtedness would result in increased fixed payment obligations and could also result in restrictive covenants, such as limitations on the Company’s ability to incur additional debt, limitations on the Company’s ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact the ability of the Company to conduct its business. If adequate funds are not available, the Company would delay, reduce or eliminate research and development programs and reduce administrative expenses. The Company may seek to access the public or private capital markets whenever conditions are favorable, even if it does not have an immediate need for additional capital at that time. In addition, if the Company raises additional funds through collaborations, strategic alliances or licensing arrangements with third parties, it may have to relinquish valuable rights to its technologies, future revenue streams or product candidates or to grant licenses on terms that may not be favorable to it. If the Company is unable to raise sufficient funding, it may be unable to continue to operate. There is no assurance that the Company will be successful in obtaining sufficient financing on acceptable terms and conditions to fund continuing operations, if at all. The failure of the Company to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on the Company’s business, results of operations and financial condition.



## 2. Significant Accounting Policies

**Basis of Presentation**—The Company’s interim financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (“GAAP”). In the opinion of management, the Company has made all necessary adjustments, which include normal recurring adjustments necessary for a fair statement of the Company’s financial position and results of operations for the interim periods presented. Certain information and disclosures normally included in the annual financial statements prepared in accordance with GAAP have been condensed or omitted. These interim financial statements should be read in conjunction with the audited financial statements and accompanying notes for the year ended December 31, 2016 included in the Company’s Annual Report on Form 10-K. The results for the three months ended March 31, 2017 are not necessarily indicative of the results to be expected for a full year, any other interim periods or any future year or period.

The accompanying consolidated financial statements include our accounts and those of our wholly-owned subsidiaries, Inotek Securities Corporation and Inotek Ltd. All significant intercompany balances and transactions have been eliminated in consolidation.

**Segment Reporting**—Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment.

**Use of Estimates**—The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Actual results could differ from these estimates. Significant items subject to such estimates and assumptions include the valuation of stock options used for the calculation of stock-based compensation and calculation of accruals related to research and clinical development.

**Comprehensive loss**—Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions, and other events and circumstances from non-owner sources, and currently consists of net loss and changes in unrealized gains and losses on short-term investments. Accumulated other comprehensive loss consists entirely of unrealized gains and losses from short-term investments as of March 31, 2017 and December 31, 2016.

**Cash and Cash Equivalents**—Cash and cash equivalents consist of bank deposits, certificates of deposit and money market accounts. Cash equivalents are carried at cost which approximates fair value due to their short-term nature and which the Company believes do not have a material exposure to credit risk. The Company considers all highly liquid investments with maturities of three months or less from the date of purchase to be cash equivalents.

The Company maintains its cash and cash equivalent balances in the form of money market, savings or operating accounts with financial institutions that management believes are creditworthy. The Company’s cash and cash equivalent accounts, at times, may exceed federally insured limits. The Company has not experienced any losses in such accounts. The Company believes it is not exposed to any significant credit risk on cash and cash equivalents.

**Short-term Investments**—Short-term investments consist of investments in certificates of deposit, agency bonds and United States Treasury securities. Management determines the appropriate classification of these securities at the time they are acquired and evaluates the appropriateness of such classifications at each balance sheet date. The Company classifies its short-term investments as available-for-sale pursuant to Financial Accounting Standards Board (“FASB”) Accounting Standard Codification (“ASC”) 320, *Investments—Debt and Equity Securities*. Short-term investments are recorded at fair value, with unrealized gains and losses included as a component of accumulated other comprehensive loss in stockholders’ equity and a component of total comprehensive loss in the consolidated statements of comprehensive loss, until realized. Realized gains and losses are included in investment income on a specific-identification basis. There were no realized gains or losses on short-term investments for the three months ended March 31, 2017 and 2016. There was \$18 of net unrealized losses on short-term investments for the three months ended March 31, 2017. There was \$11 of net unrealized gains on short-term investments for the three months ended March 31, 2016.

The Company reviews short-term investments for other-than-temporary impairment whenever the fair value of a short-term investment is less than the amortized cost and evidence indicates that a short-term investment’s carrying amount is not recoverable within a reasonable period of time. Other-than-temporary impairments of investments are recognized in the consolidated statements of operations if the Company has experienced a credit loss, has the intent to sell the short-term investment, or if it is more likely than not that the Company will be required to sell the short-term investment before recovery of the amortized cost basis. Evidence considered in this assessment includes reasons for the impairment, compliance with the Company’s investment policy, the severity and the duration of the impairment and changes in value subsequent to the end of the period.

Short-term investments at March 31, 2017 consist of the following:

	Cost Basis	Unrealized Gains	Unrealized Losses	Fair Value
<b>Current:</b>				
Certificates of deposit	\$ 22,313	\$ —	\$ —	\$ 22,313
Agency bonds	5,912	—	(6)	5,906
United States Treasury securities	61,279	—	(66)	61,213
	<u>\$ 89,504</u>	<u>\$ —</u>	<u>\$ (72)</u>	<u>\$ 89,432</u>

Short-term investments at December 31, 2016 consist of the following:

	Cost Basis	Unrealized Gains	Unrealized Losses	Fair Value
<b>Current:</b>				
Certificates of deposit	\$ 22,046	\$ —	\$ —	\$ 22,046
Agency bonds	5,917	—	(4)	5,913
United States Treasury securities	68,766	1	(51)	68,716
	<u>\$ 96,729</u>	<u>\$ 1</u>	<u>\$ (55)</u>	<u>\$ 96,675</u>

At March 31, 2017 and December 31, 2016, all short-term investments held by the Company had contractual maturities of less than one year. The Company evaluated its securities for other-than-temporary impairment and determined that no such impairment existed at March 31, 2017 and December 31, 2016.

**Property and Equipment**—Property and equipment are stated at cost. Expenditures for repairs and maintenance are charged to expense as incurred. Upon retirement or sale, the cost of the assets disposed of and the related accumulated depreciation are eliminated from the accounts and any resulting gain or loss is reflected in the consolidated statement of operations. Depreciation and amortization is provided using the straight-line method over the estimated useful lives of the assets.

**Debt Issuance Costs**—Debt issuance costs consist of underwriting discounts and offering-related costs incurred by the Company in connection with the closing of the 2021 Convertible Notes and are included as a direct deduction from the carrying amount of the 2021 Convertible Notes on the Company's consolidated balance sheets. The Company amortizes debt issuance costs to interest expense over the life of the 2021 Convertible Notes using the effective interest method. (See Note 5). Amortization of debt issuance costs was \$139 in the three months ended March 31, 2017.

**Research and Development Costs**—Research and development costs are charged to expense as incurred and include, but are not limited to:

- employee-related expenses including salaries, benefits, travel and stock-based compensation expense for research and development personnel;
- expenses incurred under agreements with contract research organizations that conduct clinical and preclinical studies, contract manufacturing organizations and consultants;
- costs associated with preclinical and development activities; and
- costs associated with regulatory operations.

Costs for certain development activities, such as clinical studies, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, and information provided to the Company by its vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the patterns of costs incurred, and are reflected in the financial statements as accrued expenses, or prepaid expenses and other current assets, if the related services have not been provided.

**Stock-Based Compensation**—The Company measures the cost of employee services received in exchange for an award of equity instruments based on the fair value of the award on the grant date. That cost is recognized on a straight-line basis over the period during which the employee is required to provide service in exchange for the award. The fair value of options on the date of grant is calculated using the Black-Scholes option pricing model based on key assumptions such as stock price, expected volatility and expected term. The Company's estimates of these assumptions are primarily based on the trading price of the Company's stock, historical data, peer company data and judgment regarding future trends and factors. The fair value of restricted stock awards is based

on the intrinsic value of such awards on the date of grant. Compensation cost for stock purchase rights under the employee stock purchase plan is measured and recognized on the date the Company becomes obligated to issue shares of our common stock and is based on the difference between the fair value of the Company's common stock and the purchase price on such date.

The Company accounts for stock options issued to non-employees in accordance with the provisions of FASB ASC 505-50, *Equity-Based Payments to Non-employees*, which requires valuing the stock options on their grant date and measuring such stock options at their current fair value as they vest.

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

Level 1—Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.

Level 2—Valuations based on quoted prices for similar assets or liabilities in markets that are not active or for which all significant inputs are observable, either directly or indirectly.

Level 3—Valuations that require inputs that reflect the Company's own assumptions that are both significant to the fair value measurement and unobservable.

To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement. The fair value of the Company's financial instruments, including cash and cash equivalents, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their respective carrying values due to the short-term nature of these instruments. The Company's assets and liabilities measured at fair value on a recurring basis include its short-term investments.

**Net Loss Per Share**—The Company calculates net loss per share in accordance with FASB ASC 260, *Earnings per Share*. Basic earnings (loss) per share ("EPS") is calculated by dividing the net income or loss applicable to common stockholders by the weighted average number of common shares outstanding for the period, without consideration of unissued common stock equivalents. The net loss applicable to common stockholders is determined by the reported net loss for the period and deducting dividends accrued and accretion of preferred stock. Diluted EPS is calculated by adjusting the weighted average common shares outstanding for the dilutive effect of common stock options, warrants, and convertible preferred stock and accrued but unpaid convertible preferred stock dividends. In periods where a net loss is recorded, no effect is given to potentially dilutive securities, as their effect would be anti-dilutive.

The following table sets forth the computation of basic and diluted EPS attributable to the Company's common stockholders:

	<u>For the Three Months Ended March 31,</u>	
	<u>2017</u>	<u>2016</u>
<b>Numerator:</b>		
Net loss applicable to common stockholders	\$ (10,670)	\$ (10,068)
<b>Denominator:</b>		
Weighted average common shares outstanding - basic and diluted	26,986,318	26,423,394
Net loss per share applicable to common stockholders - basic and diluted	<u>\$ (0.40)</u>	<u>\$ (0.38)</u>

The following common stock equivalents were excluded from the calculation of diluted net loss per share for the periods indicated as including them would have an anti-dilutive effect:

	<b>Three Months Ended March 31,</b>	
	<b>2017</b>	<b>2016</b>
Shares issuable upon conversion of the 2021 Convertible Notes	6,483,791	—
Warrants exercisable for common stock	56,408	56,408
Stock options	2,571,819	2,400,177
Restricted Stock Units	1,341,000	—
<b>Total</b>	<b>10,453,018</b>	<b>2,456,585</b>

**Subsequent Events**—The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the financial statements to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. The Company has completed an evaluation of all subsequent events through the date the financial statements were issued.

**Recent Accounting Pronouncements**—In February 2016, the FASB issued Accounting Standards Update (“ASU”) 2016-02, *Leases (Topic 842)*, which supersedes the current leasing guidance and upon adoption, will require lessees to recognize right-of-use assets and lease liabilities on the balance sheet for all leases with terms longer than 12 months. The new standard is effective for the Company for the annual period beginning after December 15, 2018, and can be early adopted by applying a modified retrospective approach for leases existing at, and entered into after, the beginning of the earliest comparable period presented in the financial statements. The Company is currently evaluating the impact of this accounting standard update on the Company’s consolidated financial statements.

In March 2016, the FASB issued ASU 2016-09, *Improvements to Employee Share-Based Payment Accounting*, which amends FASB ASC Topic 718, *Compensation – Stock Compensation (“ASC 718”)*, and includes provisions intended to simplify various aspects related to how share-based payments are accounted for and presented in the financial statements. The new standard is effective for the Company for the annual period beginning after December 15, 2016, and for annual and interim periods thereafter, with early adoption permitted. The Company adopted this standard on January 1, 2017.

The update revises requirements in the following areas: minimum statutory withholding, accounting for income taxes, and forfeitures. Prior to adoption, the Company applied a 0% forfeiture rate to share-based compensation, resulting in no cumulative effect adjustment to the opening period. Upon adoption of ASU 2016-09, the Company’s accounting policy is to recognize forfeitures as they occur. The update also requires the Company to recognize the income tax effect of awards in the income statement when the awards vest or are settled. Finally, the update allows the Company to repurchase more of an employee’s shares than it can today for tax withholding purposes without triggering a liability. The income tax related items had no effect on the current period presentation and the Company maintains a full valuation allowance against its deferred tax assets.

### 3. Property and Equipment

At March 31, 2017 and December 31, 2016, the Company’s property and equipment consisted of the following:

	<b>Useful lives</b>	<b>March 31, 2017</b>	<b>December 31, 2016</b>
Office equipment	5 years	\$ 357	\$ 407
Computer hardware and software	3 - 7 years	96	263
Laboratory equipment	5 years	499	446
Leasehold improvements	7 years	445	445
<b>Total</b>		<b>1,397</b>	<b>1,561</b>
Less: accumulated depreciation		(275)	(431)
<b>Property and equipment, net</b>		<b>\$ 1,122</b>	<b>\$ 1,130</b>

During the three months ended March 31, 2017, the Company recognized \$61 of depreciation expense and wrote off \$217 of fully depreciated net assets. During the three months ended March 31, 2016, the Company recognized \$37 of depreciation expense.

#### 4. Accrued Expenses and Other Current Liabilities

At March 31, 2017 and December 31, 2016, the Company's accrued expenses and other current liabilities consisted of the following:

	March 31, 2017	December 31, 2016
Compensation and benefits	\$ 1,216	\$ 2,171
Research and development	558	1,148
Government payable	485	478
Professional fees	231	311
Other	396	308
Total	<u>\$ 2,886</u>	<u>\$ 4,416</u>

#### 5. Debt

##### 2021 Convertible Notes

On August 5, 2016, the Company issued an aggregate of \$50,000 of the 2021 Convertible Notes. On August 30, 2016, the Company issued an additional \$2,000 of 2021 Convertible Notes pursuant to the exercise of the underwriters' overallotment option. The 2021 Convertible Notes have a maturity date of August 1, 2021 ("Maturity Date"), are unsecured and accrue interest at a rate of 5.75% per annum, payable semi-annually on February 1 and August 1 of each year, beginning February 1, 2017. In connection with the issuance of the 2021 Convertible Notes, the Company incurred \$3,262 of debt issuance costs which were recorded as a discount on the 2021 Convertible Notes.

Each holder of a 2021 Convertible Note (the "Holder") has the option until the close of business on the second business day immediately preceding the Maturity Date to convert all, or any portion, of the 2021 Convertible Notes held by it at an initial conversion rate of 124.7505 shares of the Company's common stock per \$1 principal amount of 2021 Convertible Notes (the "Conversion Rate"). The Conversion Rate is subject to adjustment from time to time upon the occurrence of certain events, including the issuance of stock dividends and payment of cash dividends. In addition, in certain circumstances, the Conversion Rate will be increased in respect of a Holder's conversion of 2021 Convertible Notes in connection with the occurrence of one or more corporate events specified in the indenture (as supplemented, the "Indenture") governing the 2021 Convertible Notes (each such specified corporate event, a "Make-Whole Fundamental Change") that occurs prior to the Maturity Date (a "Make-Whole Fundamental Change Conversion") or in respect of a Holder's voluntary conversion of 2021 Convertible Notes other than in connection with a Make-Whole Fundamental Change (a "Voluntary Conversion"). In connection with a Make-Whole Fundamental Change Conversion or a Voluntary Conversion, the Company will increase the Conversion Rate for the 2021 Convertible Notes surrendered for conversion by a number of additional shares of the Company's common stock set forth in the Additional Shares Make-Whole Table in the Indenture, based on the applicable Stock Price (as defined in the Indenture) and Effective Date (as defined in the Indenture) for such conversion. The additional shares potentially issuable in connection with a Make-Whole Fundamental Change Conversion or a Voluntary Conversion range from 0 to 24.95 per \$1 principal amount of 2021 Convertible Notes, subject to adjustment. If the Stock Price applicable to any conversion is greater than \$40.00 per share, the Conversion Rate will not be increased. If the Stock Price applicable to any conversion is less than \$6.68 per share, the Conversion Rate in connection with a Make-Whole Fundamental Change Conversion will not be increased but it will be increased by 24.95 shares in connection with a Voluntary Conversion. Upon conversion, Holders of the 2021 Convertible Notes will receive shares of the Company's common stock and cash in lieu of fractional shares.

Upon the occurrence of a Fundamental Change, the occurrence of certain change of control transactions or delisting events (as defined in the Indenture), each Holder may require the Company to repurchase for cash all or any portion of the 2021 Convertible Notes held by such Holder at a repurchase price equal to 100% of the principal amount thereof, plus accrued and unpaid interest thereon.

The Company, at its option, may redeem for cash all or any portion of the 2021 Convertible Notes if the last reported sale price of a share of the Company's common stock is equal to or greater than 200% of the conversion price for the 2021 Convertible Notes then in effect for at least 20 trading days (whether or not consecutive) during any 30 consecutive trading day period (including the last trading day of such period) ending within the five trading days immediately preceding the date on which the Company provides notice of redemption, at a redemption price equal to 100% of the principal amount of the 2021 Convertible Notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date.

If an Event of Default (as defined in the Indenture), other than certain events of bankruptcy, insolvency or reorganization involving the Company, occurs and is continuing, the trustee under the Indenture (the "Trustee") or the Holders of at least 25% in principal amount of the outstanding 2021 Convertible Notes may declare 100% of the principal of and accrued and unpaid interest, if any, on all of the 2021 Convertible Notes to be due and payable immediately. Upon the occurrence of an Event of Default relating to bankruptcy, insolvency or reorganization involving the Company, 100% of the principal of and accrued and unpaid interest, if any, on all of the 2021 Convertible Notes would become due and payable automatically.

Notwithstanding the foregoing, the Indenture provides that, to the extent the Company elects, the sole remedy for an Event of Default relating to certain failures by the Company to comply with certain reporting covenants in the Indenture, will (i) for the first 90 days after the occurrence of such an Event of Default, consist exclusively of the right to receive additional interest on the 2021 Convertible Notes at a rate equal to 0.25% per annum of the principal amount of the 2021 Convertible Notes outstanding for each day during such 90-day period on which such an Event of Default is continuing and (ii) for the period from, and including, the 91st day after the occurrence of such an Event of Default to, and including, the 180th day after the occurrence of such an Event of Default, consist exclusively of the right to receive additional interest on the 2021 Convertible Notes at a rate equal to 0.50% per annum of the principal amount of the 2021 Convertible Notes outstanding for each day during such additional 90-day period on which such an Event of Default is continuing (such additional interest, “Additional Interest”). After 180 days, if such Event of Default is not cured or waived, the 2021 Convertible Notes would be subject to acceleration in accordance with the Indenture.

The 2021 Convertible Notes are considered a hybrid financial instrument consisting of a fixed interest rate “host” and various embedded features that required evaluation as potential embedded derivatives under FASB ASC 815, *Derivatives and Hedging* (“ASC 815”). Based on the nature of the host instrument and the embedded features, management concluded that none of the conversion, put and redemption features required bifurcation and separate accounting from the host instrument. The Company determined that the Additional Interest was an embedded derivative that contains non-credit related events of default. As a result, the Additional Interest feature required bifurcation and separate accounting under ASC 815. Based on the amount of Additional Interest that would be owed and the likelihood of occurrence, the Company estimated the fair value of the Additional Interest feature to be insignificant as of March 31, 2017 and December 31, 2016.

The issuance costs which were recorded as a discount on the debt are being amortized to interest expense over the life of the 2021 Convertible Notes using the effective interest method. As of March 31, 2017, the stated interest rate was 5.75%, and the effective interest rate was 7.3%. Interest expense related to the 2021 Convertible Notes for the three months ended March 31, 2017, was \$876, including \$139 related to amortization of the debt discount.

The table below summarizes the carrying value of the 2021 Convertible Notes as of March 31, 2017:

	<b>March 31, 2017</b>
Gross proceeds	\$ 52,000
Initial value of issuance costs recorded as debt discount	(3,262)
Amortization of debt discount	361
Carrying value	<u>\$ 49,099</u>

## 6. Equity

### *Authorized Shares*

As of March 31, 2017, the Company’s authorized capital stock consisted of 120,000,000 shares of common stock, par value \$0.01 per share, and 5,000,000 shares of undesignated preferred stock, par value \$0.001 per share.

### *Common Stock*

All preferences, voting powers, relative, participating, optional, or other specific rights and privileges, limitations, or restrictions of the common stock are expressly subject to those that may be fixed with respect to any shares of preferred stock. Common stockholders are entitled to one vote per share, and to receive dividends, when and if declared by the Company’s board of directors. At March 31, 2017 and December 31, 2016, there were 26,986,318 shares of common stock outstanding.

### *Equity Plans*

The Company maintains three equity compensation plans: the 2014 Stock Option and Incentive Plan (the “2014 Plan”), the 2004 Stock Option and Incentive Plan (the “2004 Plan”) and the 2014 Employee Stock Purchase Plan (“ESPP”).

#### *2014 Stock Option and Incentive Plan*

The 2014 Plan provides for the issuance of incentive and non-qualified stock options, restricted stock, and other equity awards, all for common stock, as determined by the board of directors to employees, officers, directors, consultants, and advisors of the Company and its subsidiaries. Pursuant to the provisions of the 2014 Plan and approval by the board of directors, on January 1, 2017 an additional 1,079,453 shares were added to the 2014 Plan representing 4% of total common shares issued and outstanding at December 31, 2016. There were 315,028 shares available for issuance under the 2014 Plan as of March 31, 2017. The 2014 Plan expires in August 2024.

In December 2016, the board granted to certain executive officers an aggregate of 470,000 RSU's pursuant to the 2014 Plan. Each restricted stock unit represents a contingent right to receive one share of Company common stock. Vesting for these RSU's was based equally on the achievement of two performance-based conditions, subject to continued service through such achievement dates. The intrinsic fair value of these RSU's as of the date of grant was \$3,055 and no stock-based compensation expense was recorded in 2016 as the Company determined that the vesting conditions were not probable of occurring. In January 2017, these RSU's were modified such that instead of vesting based on the achievement of certain performance-based conditions, they will vest in equal annual installments over four years from the December 2016 date of grant, subject to continued service through such dates. This change in vesting criteria was accounted for as a modification under ASC 718 whereby the Company will recognize the \$717 fair value of the grants as of the date of modification over the vesting term.

The following table summarizes stock option activity under the 2014 Plan:

	<u>Number of Shares</u>	<u>Weighted Average Exercise Price Per Share</u>	<u>Aggregate Intrinsic Value</u>
Outstanding at December 31, 2016	2,664,832	\$ 6.16	
Granted	—		
Exercised	—		
Cancelled	(103,542)	\$ 7.49	
Outstanding at March 31, 2017	<u>2,561,290</u>	\$ 6.11	\$ —
Exercisable at March 31, 2017	<u>1,146,966</u>	\$ 5.51	\$ —
Weighted-average years remaining on contractual life	8.24		
Unrecognized compensation cost related to non-vested stock options	\$ 7,170		

The exercise prices exceed the \$2.00 per share closing price of common stock on March 31, 2017, therefore there is no intrinsic value of the outstanding 2014 Plan stock options.

The following table summarizes RSU activity under the 2014 Plan:

	<u>Number of Shares</u>	<u>Weighted Average Grant Date Fair Value Per Share</u>
Outstanding at December 31, 2016	470,000	\$ 6.50
Granted	931,000	\$ 1.60
Vested	—	
Cancelled	(60,000)	\$ 1.70
Outstanding at March 31, 2017	<u>1,341,000</u>	\$ 1.57

The weighted average grant date fair value per share of outstanding RSU's as of March 31, 2017 reflects the \$1.53 per share fair value of the modified RSU's as of the date of modification.

## 2004 Stock Option and Incentive Plan

The following table summarizes stock option activity under the 2004 Plan:

	<u>Number of Shares</u>	<u>Weighted Average Exercise Price Per Share</u>	<u>Aggregate Intrinsic Value</u>
Outstanding at December 31, 2016	10,626	\$ 40.58	
Exercised	—		
Expired	(97)	\$ 40.58	
Cancelled	—		
Outstanding at March 31, 2017	<u>10,529</u>	\$ 40.58	\$ —
Exercisable at March 31, 2017	<u>10,529</u>	\$ 40.58	\$ —
Weighted-average years remaining on contractual life	1.01		
Unrecognized compensation cost related to non-vested stock options	\$ —		

The exercise prices exceed the \$2.00 per share closing price of common stock on March 31, 2017, therefore there is no intrinsic value of the outstanding 2004 Plan stock options.

## Employee Stock Purchase Plan

In November 2014, the Company's board of directors adopted and the stockholders approved the 2014 Employee Stock Purchase Plan ("ESPP"). The ESPP provides that the number of shares reserved and available for issuance under the ESPP shall be cumulatively increased each January 1, beginning on January 1, 2016, by the lesser of (i) 600,000 shares of common stock or (ii) the number of shares necessary to set the number of shares of Common Stock under the Plan at 1% percent of the outstanding number of shares as of January 1 of the applicable year. However, the board of directors reserves the right to determine that there will be no increase for any year or that any increase will be for a lesser number of shares. As of January 1, 2017, 31,555 shares were added to the ESPP. As of March 31, 2017, there were 269,863 shares available for issuance under the ESPP. The Company recorded \$18 and \$20 of stock-based compensation expense pursuant to the ESPP during the three months ended March 31, 2017 and 2016, respectively.

## Stock-Based Compensation

Stock-based compensation expense for options, restricted stock units ("RSU's") and the ESPP is reflected in the consolidated statements of operations as follows:

	<u>Three Months Ended March 31,</u>	
	<u>2017</u>	<u>2016</u>
Research and development	\$ 303	\$ 209
General and administrative	481	277
Total	<u>\$ 784</u>	<u>\$ 486</u>

## 7. Commitments and Contingencies

### Operating lease

In 2015, the Company entered into a lease agreement (the "Office Lease") for its headquarters in Lexington, Massachusetts. The Company recorded \$445 as leasehold improvements for costs incurred to build out the space, and is amortizing those costs to facilities expense over the term of the lease. Rent expense is recognized on a straight-line basis at the average monthly rent over the term of the lease. Deferred rent is included in other current and long-term liabilities on the Company's consolidated balance sheets.



In 2016, the Company signed an amendment to the Office Lease, whereby it agreed to rent additional space (the “Lease Amendment”). The terms of the Lease Amendment follow the terms of the Office Lease. The lease term is 90 months and the Company has the right to extend the term for one period of five years.

Rent expense was \$84 and \$62 for the three months ended March 31, 2017 and 2016, respectively. As of March 31, 2017, the aggregate annual commitments pursuant to the Office Lease and the Lease Amendment are as follows:

Year	Amount
2017	\$ 302
2018	411
2019	421
2020	429
2021	439
Thereafter	520
<b>Total</b>	<b>\$ 2,522</b>

### Securities Litigation

On January 6, 2017, a purported stockholder of the Company filed a putative class action in the U.S. District Court for the District of Massachusetts, against the Company, David Southwell, Rudolf Baumgartner, Dale Ritter, and William McVicar, captioned Whitehead v. Inotek Pharmaceuticals Corporation, et al., No. 1:17-cv-10025. The complaint alleges violations of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and SEC Rule 10b-5 based on allegedly false and misleading statements and omissions regarding our MATrX-1 phase 3 clinical trial of *trabodenson*. The lawsuit seeks among other things, unspecified compensatory damages, interest, attorneys’ fees and costs, and unspecified equitable/injunctive relief. The Company intends to vigorously defend itself against this claim.

### Indemnification Arrangements

As permitted under Delaware law, the Company’s bylaws provide that the Company will indemnify any director, officer, employee or agent of the Company or anyone serving in these capacities. The maximum potential amount of future payments the Company could be required to pay is unlimited. The Company has insurance that reduces its monetary exposure and would enable it to recover a portion of any future amounts paid. As a result, the Company believes that the estimated fair value of these indemnification commitments is minimal.

Throughout the normal course of business, the Company has agreements with vendors that provide goods and services required by the Company to run its business. In some instances, vendor agreements include language that requires the Company to indemnify the vendor from certain damages caused by the Company’s use of the vendor’s goods and/or services. The Company has insurance that would allow it to recover a portion of any future amounts that could arise from these indemnifications. As a result, the Company believes that the estimated fair value of these indemnification commitments is minimal.

## 8. Fair Value of Financial Measurements

Items measured at fair value on a recurring basis are short-term investments. The following table sets forth the Company’s financial instruments that were measured at fair value on a recurring basis by level within the fair value hierarchy:

	Fair Value Measurements at March 31, 2017			
	Total	Level 1	Level 2	Level 3
<b>Assets:</b>				
Money market mutual funds (included in cash and cash equivalents)	\$ 13,090	\$ 13,090	\$ —	\$ —
Certificates of deposit	\$ 22,313	\$ —	\$ 22,313	\$ —
Agency bonds	5,906	—	5,906	—
United States Treasury securities	61,213	61,213	—	—
Short-term investments	\$ 89,432	\$ 61,213	\$ 28,219	\$ —

**Fair Value Measurements at  
December 31, 2016**

	<u>Total</u>	<u>Level 1</u>	<u>Level 2</u>	<u>Level 3</u>
<b>Assets:</b>				
Money market mutual funds (included in cash and cash equivalents)	\$ 20,698	\$ 20,698	\$ —	\$ —
Certificates of deposit	\$ 22,046	\$ —	\$ 22,046	\$ —
Agency bonds	5,913	—	5,913	—
United States Treasury securities	68,716	68,716	—	—
Short-term investments	\$ 96,675	\$ 68,716	\$ 27,959	\$ —

***Money market mutual funds***

The Company classifies its money market mutual funds as Level 1 assets under the fair value hierarchy as these assets have been valued using quoted market prices in active markets without any valuation adjustment.

***Short-term investments***

The Company classifies its United States Treasury securities as Level 1 assets under the fair value hierarchy as these assets have been valued using quoted market prices in active markets without any valuation adjustment. The Company classifies its certificates of deposit as Level 2 assets under the fair value hierarchy, as there are no quoted market prices in active markets, and its agency bonds as Level 2 assets under the fair value hierarchy, as these assets are not always valued daily using quoted market prices in active markets.

## Item 2. Management’s Discussion and Analysis of Financial Condition and Results of Operations

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our condensed financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q and our Annual Report on Form 10-K for the fiscal year ended December 31, 2016.

### 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 (“IOP”). Our lead product candidate, *trabodенoson*, is a first-in-class selective adenosine mimetic that we rationally designed to lower IOP by restoring the eye’s natural pressure control mechanism. Our product pipeline includes *trabodенoson* monotherapy delivered in an eye drop formulation, as well as a fixed-dose combination (“FDC”) of *trabodенoson* with *latanoprost*, a prostaglandin analogue (“PGA”), given once-daily. Our completed Phase 2 trial of *trabodенoson* co-administered with *latanoprost* demonstrated IOP-lowering in patients who have previously had inadequate response 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.

On January 3, 2017, we announced top-line results of MATrX-1, the first pivotal Phase 3 trial of *trabodенoson* for the treatment of primary open-angle glaucoma or ocular hypertension. The trial did not meet its primary endpoint because it did not demonstrate a statistically significant difference in absolute IOP from placebo at every single one of the 12 time points comprising the primary endpoint. This was due to a larger than expected treatment effect in the placebo/vehicle group, as compared to both our prior Phase 2 data and a recent meta-analysis examining placebo responses from 10 placebo-controlled trials, which showed a placebo/vehicle result of -2.01 mmHg (Raber, et al). During analysis of the IOP data from the trial, a treatment-by-site interaction was found where a small number of sites (4 sites out of a total of 55) caused an important change in the expected vehicle results. MATrX-1 did achieve several clinically meaningful secondary endpoints - the 6% dose was significant versus placebo in the daily IOP change from diurnal baseline at all days tested. Additionally, an analysis of responders (subjects with IOP reduction of 5mmHg or greater from baseline) indicated a statistically higher proportion of responders in the 6% *trabodенoson* group than the placebo group at all visits. There were no significant safety or tolerability events reported. The safety profile of *trabodенoson* was comparable to placebo and there was minimal drug related hyperemia. The U.S. Food and Drug Administration (the “FDA”) has communicated to us their agreement with these results.

In July 2016, we announced the initiation of a Phase 2 dose-ranging trial of a fixed-dose combination (“FDC”) of *trabodенoson* and *latanoprost*. The trial will enroll approximately 200 patients with an IOP greater than or equal to 25 mmHg and less than or equal to 34 mmHg; which represents the patients most likely to receive treatment for glaucoma or ocular hypertension. In April 2017, we announced the completion of active enrollment for this trial. Data from this trial is expected in July 2017.

In April 2016, we filed a registration statement on Form S-3 containing two prospectuses: (i) a base prospectus which covers the offering, issuance and sale by us of up to \$200.0 million in the aggregate of an indeterminate number of shares of common stock and preferred stock, such indeterminate principal amount of debt securities and such indeterminate number of warrants and; and (ii) a sales agreement prospectus covering the offering, issuance and sale by us of up to a maximum aggregate offering price of \$50.0 million of our common stock that may be issued and sold under an at-the-market sales agreement with Cowen and Company, LLC (the “ATM”). The \$50.0 million of common stock that may be issued and sold under the ATM reduces the available balance under the base prospectus by the amount issued. We did not sell any shares of common stock pursuant to the ATM during the three months ended March 31, 2017. At March 31, 2017, \$45.6 million was available for sale of common stock under the ATM. Additionally, in 2016 we issued \$52.0 million aggregate principal amount of 5.75% Convertible Senior Notes due 2021 pursuant to a Prospectus Supplement to our Form S-3, (the “2021 Convertible Notes”), which further reduces the balance available under the base prospectus to \$98.0 million as of March 31, 2017.

As of March 31, 2017, we had an accumulated deficit of \$249.5 million and cash and cash equivalents and short-term investments aggregating \$114.7 million. We estimate we have sufficient funding to sustain operations into 2019. See “Liquidity and Capital Resources.”

Since our inception on July 7, 1999, we have devoted substantially all of our resources to business planning, raising capital, product research and development, applying for and obtaining government and private grants, recruiting management, research and technical staff and other personnel, acquiring operating assets, and undertaking preclinical studies and clinical trials of our lead product candidates. We have not completed development of any product candidate and we have therefore not generated any revenues from product sales.

## Factors Affecting our Results of Operations

The review of MATrX-1 data is ongoing and results from our ongoing Phase 2 trial with our FDC product candidate are expected in July 2017. We are also analyzing *trabodenson*'s utility beyond the lowering of eye pressure, including its neuroprotective activity in the back of the eye. Additionally, we are evaluating the potential for selective adenosine mimetics to address optic neuropathies and other degenerative retinal diseases and to improve the pathophysiology associated with dry eye disease. We do not expect our aggregate research and development expenses to increase in 2017 over 2016. If we successfully develop and launch *trabodenson* as a monotherapy or any other product candidates, we expect to incur significant commercialization expenses related to sales, marketing, manufacturing and distribution of our products.

We will need to obtain additional funding in connection with our continuing operations. Adequate additional financing may not be available to us on acceptable terms, or at all. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or any potential future commercialization efforts. We will need to generate significant revenues to achieve profitability, and we may never do so. As a result, we expect to incur significant expenses and operating losses for the foreseeable future.

## Financial Overview

### Revenue

We have not generated any revenue from product sales since our inception and do not expect to generate any revenue from the sale of products in the near future. Our ability to generate revenues will depend on the successful development, regulatory approval and commercialization of *trabodenson* and any other future product candidates.

### Research and Development Expenses

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

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

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

The following table summarizes our research and development expenses by type of activity for the three months ended March 31, 2017 and 2016:

	For the Three Months Ended March 31,	
	2017	2016
	(in thousands)	
Trabodenoson - direct clinical and non-clinical	\$ 4,630	\$ 5,823
Personnel and other expenses		
Employee and consultant-related expenses	1,769	1,561
Facility expenses	154	124
Target validation expenses	487	-
Other expenses	57	107
Total personnel and other expenses	2,467	1,792
Total research and development expenses	\$ 7,097	\$ 7,615

We do not track *trabodenoson*-related expenses by product candidate. All expenses related to *trabodenoson* as a monotherapy also benefit the FDC product candidate *trabodenoson* with *latanoprost*. We have expended approximately \$79 million for external development costs related to *trabodenoson* from inception through March 31, 2017.

The process of conducting the necessary clinical research to obtain regulatory approval is costly and time consuming and the successful development of our product candidates is highly uncertain, especially considering the MATrX-1 Phase 3 clinical trial's failure to meet its primary endpoint. Our future research and development expenses will depend on the clinical success of our product candidates, as well as ongoing assessments of the commercial potential of such product candidates. In addition, we cannot forecast with any degree of certainty which product candidates may be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements.

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

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

A change in the outcome of any of these variables with respect to the development of *trabodenoson* or any other product candidate that we may develop could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials or other testing beyond those that we currently contemplate for the completion of clinical development of *trabodenoson* or any other product candidate that we may develop or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development of that product candidate.

As a result of the uncertainties discussed above, we are unable to determine with certainty the duration and completion costs of our development programs or precisely when and to what extent we will receive revenue from the commercialization and sale of our product candidates. We may never succeed in achieving regulatory approval for one or more of our product candidates. The duration, costs and timing of clinical trials and development of any product candidates will depend on a variety of factors, including the uncertainties of future preclinical studies and clinical trials, uncertainties in the clinical trial enrollment rate and changing government regulation. In addition, the probability of success for each product candidate will depend on numerous factors, including efficacy and tolerability profiles, manufacturing capability, competition, and commercial viability.

### **General and Administrative Expenses**

General and administrative expenses consist of compensation and related benefit costs, including stock-based compensation for administrative personnel. Other significant general and administrative expenses include travel costs, professional fees for legal, patents, consulting, investor and public relations, auditing and tax services as well as other direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies used in general and administrative activities.

### **Interest Expense**

Interest expense in 2017 relates to our 2021 Convertible Notes which are due in August 2021.

### **Interest Income**

Interest income relates to interest earned from invested funds.

## **Results of Operations**

### **Comparison of the Three Months Ended March 31, 2017 and 2016**

The following table summarizes the results of our operations for the three months ended March 31, 2017 and 2016:

(in thousands)	Three Months Ended March 31,		Increase (Decrease)
	2017	2016	
Operating expenses:			
Research and development	\$ (7,097)	\$ (7,615)	\$ (518)
General and administrative	(2,869)	(2,522)	347
Loss from operations	\$ (9,966)	\$ (10,137)	\$ (171)
Interest expense	(876)	-	876
Interest income	172	69	(103)
Net loss	<u>\$ (10,670)</u>	<u>\$ (10,068)</u>	<u>\$ 602</u>

### **Research and development expenses**

Research and development expenses decreased \$0.5 million to \$7.1 million for the three months ended March 31, 2017, as compared to \$7.6 million for the three months ended March 31, 2016. This decrease primarily reflects \$3.1 million of decreased clinical expenses related to the completion of our Phase 3 trial, MATrX-1, in January of 2017, partially offset by \$1.7 million of increased clinical expenses related to our Phase 2 trial with our FDC product candidate that commenced in October 2016. In addition, we had \$0.6 million of increased preclinical activities and \$0.2 million of increased employee-related expenses due to increased headcount and additional stock option grants.

### **General and administrative expenses**

General and administrative expenses increased \$0.4 million to \$2.9 million for the three months ended March 31, 2017, as compared to \$2.5 million for the three months ended March 31, 2016. This increase primarily reflects \$0.2 million related to increased employee-related expenses due to increased headcount and additional stock option grants.

### **Interest expense**

Interest expense in 2017 relates to coupon interest and amortization of debt issuance costs related to our 2021 Convertible Notes which are due in August 2021.

### Interest income

Interest income increased \$0.1 million to \$0.2 million for the three months ended March 31, 2017, as compared to \$0.1 million for the three months ended March 31, 2016. This increase primarily reflects higher weighted average invested balances and interest rates.

### Liquidity and Capital Resources

Since inception, we have incurred accumulated net losses and negative cash flows from our operations. We incurred a net loss of \$10.7 million for the three months ended March 31, 2017. As of March 31, 2017, we had an accumulated deficit of \$249.5 million and \$114.7 million of cash and cash equivalents and short-term investments. We are obligated to pay approximately \$1.5 million of interest on the 2021 Convertible Notes on each February 1 and August 1 of 2017 through 2021, and on August 1, 2021 the full outstanding principal, currently \$52.0 million, is due and payable.

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

	Three Months Ended March 31,	
	2017	2016
	(in thousands)	
Cash used in operating activities	\$ (11,619)	\$ (8,993)
Cash provided by (used in) investing activities	7,094	(12,343)
Cash provided by financing activities	—	—
Net increase (decrease) in cash and cash equivalents	<u>\$ (4,525)</u>	<u>\$ (21,336)</u>

#### Net cash used in operating activities

Net cash used in operating activities was \$11.6 million for the three months ended March 31, 2017 and \$9.0 million for the three months ended March 31, 2016. Net cash used in operating activities for the three months ended March 31, 2017, principally resulted from our net loss of \$10.7 million and a \$2.0 million net change in operating assets and liabilities, partially offset by \$0.8 million in noncash stock-based compensation.

Net cash used in operating activities for the three months ended March 31, 2016, principally resulted from our net loss of \$10.1 million, partially offset by \$0.5 million in noncash stock-based compensation, a \$0.5 million increase in accrued expenses and accounts payable and a \$0.1 million increase in prepaid expenses.

#### Net cash provided by (used in) investing activities

Net cash provided by investing activities was \$7.1 million for the three months ended March 31, 2017, and related primarily to \$19.9 million of proceeds from the maturity of short-term investments, partially offset by the purchase of \$12.7 million of short-term investments.

Net cash used in investing activities was \$12.3 million for the three months ended March 31, 2016, and related primarily to the purchase of \$24.2 million of short-term investments and \$11.8 million of proceeds from the maturity of short-term investments.

#### Operating Capital Requirements

To date, we have not generated any revenue from product sales. We do not know when, or if, we will generate any revenue from product sales. We do not expect to generate significant revenue from product sales unless and until we obtain regulatory approval of and commercialize one of our current or future product candidates. We anticipate that we will continue to generate losses for the foreseeable future and we expect the losses to increase as we continue the development of, and seek regulatory approvals for, our product candidates and begin to commercialize any approved products. Since the closing of our IPO in February 2015, we are incurring additional costs associated with operating as a public company. In addition, subject to obtaining regulatory approval of any of our product candidates, we expect to incur significant commercialization expenses for product sales, marketing and manufacturing. Accordingly, we anticipate that we will need substantial additional funding in connection with our continuing operations.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. To the extent that we are able to raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and may require the issuance of warrants, which could cause potential dilution. If we raise additional funds through collaborations, strategic alliances or

licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or research programs or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

### Contractual Obligations and Commitments

The following summarizes our significant contractual obligations as of March 31, 2017:

	Total	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years
	(in thousands)				
Operating facilities lease (1)	\$ 2,522	\$ 404	\$ 836	\$ 873	\$ 409
2021 Convertible Notes (2)	65,455	2,990	5,980	56,485	-
Total	\$ 67,977	\$ 3,394	\$ 6,816	\$ 57,358	\$ 409

(1) Represents lease payments for our headquarters in Lexington, Massachusetts.

(2) Represents principal and interest payments on our 2021 Convertible Notes.

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

### JOBS Act

Under Section 107(b) of the Jumpstart Our Business Startups Act of 2012 (the “JOBS Act”), an “emerging growth company” can delay the adoption of new or revised accounting standards until such time as those standards would apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and, as a result, we will adopt new or revised accounting standards at the same time as other public companies that are not emerging growth companies. There are other exemptions and reduced reporting requirements provided by the JOBS Act that we are currently evaluating. For example, as an emerging growth company, we are exempt from Sections 14A(a) and (b) of the Securities Exchange Act of 1934 (the “Exchange Act”) which would otherwise require us to (i) submit certain executive compensation matters to stockholder advisory votes, such as “say-on-pay,” “say-on-frequency” and “golden parachutes” and (ii) disclose certain executive compensation related items such as the correlation between executive compensation and performance and comparisons of our Chief Executive Officer’s compensation to our median employee compensation. We also intend to rely on an exemption from the rule requiring us to provide an auditor’s attestation report on our internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and the rule requiring us to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board (“PCAOB”) regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements as the auditor discussion and analysis. We will continue to remain an “emerging growth company” until the earliest of the following: December 31, 2020; the last day of the fiscal year in which our total annual gross revenue is equal to or more than \$1.07 billion; the date on which we have issued more than \$1 billion in nonconvertible debt during the previous three years; or the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

### Off-Balance Sheet Arrangements

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

### Item 3. Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risks in the ordinary course of our business. These market risks are principally limited to interest rate fluctuations. We had cash and cash equivalents of \$25.3 million at March 31, 2017, consisting primarily of funds in money market accounts. We also had \$89.4 million in short-term investments consisting of certificates of deposit, agency bonds and United States Treasury securities. The primary objective of our investment activities is to preserve principal and liquidity while maximizing income without significantly increasing risk. We do not enter into investments for trading or speculative purposes. Due to the short-term nature of our investment portfolio, we do not believe an immediate 1.0% increase in interest rates would have a material effect on the



fair market value of our portfolio, and accordingly we do not expect a sudden change in market interest rates to affect materially our operating results or cash flows.

#### **Item 4. Controls and Procedures**

##### ***Evaluation of Disclosure Controls and Procedures***

Our management, with the participation of our principal executive officer and our principal financial officer, evaluated, as of the end of the period covered by this Quarterly Report on Form 10-Q, the effectiveness of our disclosure controls and procedures. Based on that evaluation of our disclosure controls and procedures as of March 31, 2017, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures as of such date are effective at the reasonable assurance level. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act are recorded, processed, summarized and reported within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial and accounting officer, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

##### ***Inherent Limitations of Internal Controls***

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

##### ***Changes in Internal Control over Financial Reporting***

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended March 31, 2017, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

## **PART II – OTHER INFORMATION**

#### **Item 1. Legal Proceedings**

On January 6, 2017, a purported stockholder of the Company filed a putative class action in the U.S. District Court for the District of Massachusetts, against the Company, David Southwell, Rudolf Baumgartner, Dale Ritter, and William McVicar, captioned *Whitehead v. Inotek Pharmaceuticals Corporation, et al.*, No. 1:17-cv-10025. The complaint alleges violations of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and SEC Rule 10b-5 based on allegedly false and misleading statements and omissions regarding our MATrX-1 phase 3 clinical trial of *trabodenason*. The lawsuit seeks among other things, unspecified compensatory damages, interest, attorneys’ fees and costs, and unspecified equitable/injunctive relief.

From time to time, we may be subject to other various legal proceedings and claims that arise in the ordinary course of our business activities. Although the results of litigation and claims cannot be predicted with certainty, we do not believe we are party to any other claim or litigation the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

## Item 1A. Risk Factors

We operate in an industry that involves numerous risks and uncertainties. You should carefully consider the following information about these risks, together with the other information appearing elsewhere in this Form 10-Q for the quarterly period ended March 31, 2017 and our Annual Report on Form 10-K for the year ended December 31, 2016, including our financial statements and related notes hereto. The occurrence of any of the following risks could have a material adverse effect on our business, financial condition, results of operations and future growth prospects. The risks and uncertainties described below may change over time and other risks and uncertainties, including those that we do not currently consider material, may impair our business. In these circumstances, the market price of our common stock could decline.

### 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 *trabodendoson* monotherapy and *trabodendoson* 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 \$42.9 million and \$68.0 million for the years ended December 31, 2016 and 2015, respectively. Our net losses were \$10.7 million and \$10.1 million for the three months ended March 31, 2017 and 2016, respectively. As of March 31, 2017, we had an accumulated deficit of \$249.5 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 or elsewhere 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.

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, or 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.

In August 2015, we completed an underwritten public offering of our common stock, or the Follow-on Offering. We issued 6,210,000 shares of our common stock at a price of \$12.75 per share, including 810,000 shares from the underwriters' full exercise of their overallotment option, and we received net proceeds of \$74.0 million, after deducting underwriting discounts and offering-related costs.

In 2016, we sold 482,689 shares of common stock pursuant to our ATM and received net proceeds of \$4.0 million.

In August 2016, we closed an underwritten public offering of \$52.0 million aggregate principal amount of 5.75% Convertible Senior Notes due 2021, including \$2.0 million from an exercise of the underwriters' overallotment option, or the 2021 Convertible Notes, and received net proceeds of approximately \$48.7 million after deducting underwriting discounts and offering-related costs. (See Note 5 in the accompanying notes to the financial statements).

We expect our research and development expenses to continue to be significant in connection with our product development activities, including our Phase 2 clinical trial for our FDC product candidate which commenced in July 2016, 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. As of March 31, 2017, our cash and cash equivalents and short-term investments aggregated \$114.7 million. We estimate that these funds will be sufficient to fund our projected operating requirements into 2019. 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 and other contractual commitments are substantial and may 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, costs and success 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.***

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.

***The indenture governing our 2021 Convertible Notes contain restrictions that will limit our operating flexibility, and we may incur additional debt in the future that may include similar or additional restrictions.***

The indenture governing our 2021 Convertible Notes contain covenants that, among other things, restrict our and our subsidiaries' ability to take specific actions, even if we believe them to be in our best interest. These covenants include restrictions on our ability and the ability of our future subsidiaries to incur additional indebtedness and issue certain types of preferred stock, other than certain permitted indebtedness and preferred stock. In addition, the indenture governing our 2021 Convertible Notes will include a covenant that limits our ability to merge or consolidate with other entities in certain circumstances. These covenants and restrictions limit our operational flexibility and could prevent us from taking advantage of business opportunities as they arise, growing our business or competing effectively.

A breach of any of these covenants or other provisions in our future debt agreements could result in an event of default, which if not cured or waived, could result in the 2021 Convertible Notes or such debt becoming immediately due and payable. This, in turn, could cause any of our other debt existing at such time to become due and payable as a result of cross-default or cross-acceleration provisions contained in the agreements governing such other debt. In the event that some or all of our debt is accelerated and becomes immediately due and payable, we may not have the funds to repay, or the ability to refinance, such debt.

***Servicing our debt requires a significant amount of cash, and we may not have sufficient cash flow from our business to pay our substantial debt.***

We currently have no source of revenue. Our ability to make scheduled payments of the principal of, to pay interest on or to refinance our indebtedness, including the 2021 Convertible Notes, depends on our future performance, which is subject to economic, financial, competitive and other factors, most of which are beyond our control. Our business has not historically generated cash flow from operating activities and may not in the future generate cash flow from operating activities sufficient to service our obligations under our 2021 Convertible Notes and any future indebtedness we may incur and to make necessary capital expenditures. If we are unable to generate such cash flow, we may be required to adopt one or more alternatives, such as reducing or delaying investments or capital expenditures, selling assets, restructuring debt or obtaining additional equity capital on terms that may be onerous or highly dilutive. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at such time. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations.

***We may not have the ability to raise the funds necessary to repurchase our 2021 Convertible Notes upon a fundamental change, and our future debt may contain limitations on our ability to repurchase the 2021 Convertible Notes.***

Holders of our 2021 Convertible Notes have the right to require us to repurchase their 2021 Convertible Notes upon the occurrence of a fundamental change, the occurrence of certain change of control transactions or delisting events, at a fundamental change repurchase price equal to 100% of the principal amount of the 2021 Convertible Notes to be repurchased, plus accrued and unpaid interest, if any, to, but not including, the fundamental change repurchase date. However, we may not have enough available cash or be able to obtain financing at the time we are required to make repurchases of 2021 Convertible Notes surrendered therefor. In addition, our ability to repurchase the 2021 Convertible Notes may be limited by law, by regulatory authority or by agreements governing our future indebtedness. Our failure to repurchase 2021 Convertible Notes at a time when the repurchase is required by the indenture would constitute a default under the indenture. A default under the indenture or the fundamental change itself could also lead to a default under agreements governing our future indebtedness, if any. If the repayment of the related indebtedness were to be accelerated after any applicable notice or grace periods, we may not have sufficient funds to repay the indebtedness and repurchase the 2021 Convertible Notes.

***The fundamental change repurchase feature of our 2021 Convertible Notes may delay or prevent an otherwise beneficial attempt to take over our company.***

The terms of our 2021 Convertible Notes require us to repurchase the 2021 Convertible Notes in cash in the event of a fundamental change. A takeover of our company, if such takeover constituted a “fundamental change,” would trigger an option of the holders of the 2021 Convertible Notes to require us to repurchase the 2021 Convertible Notes. This may have the effect of delaying or preventing a takeover of our company that would otherwise be beneficial to investors in the 2021 Convertible Notes.

## **Risks Related to Development, Potential Regulatory Approval and Commercialization**

***We depend substantially on the success of our product candidates, particularly trabodenson monotherapy and trabodenson FDC, which are still in development. We may be unable to successfully develop and commercialize our product candidates, especially in light of our MATrX-1 clinical trial’s failure to meet its primary endpoint, or may experience significant delays in doing so, which would materially harm our business.***

Our business and the ability to generate revenue related to product sales, if ever, will depend on the successful development, formulation and manufacturing, regulatory approval and commercialization of our product candidates *trabodenson* monotherapy and *trabodenson* FDC, which are still in development, and other potential products we may develop or license. In January 2017, we announced top-line data from our MATrX-1 pivotal Phase 3 clinical trial, which failed to meet its primary endpoint. MATrX-1 did not meet its primary endpoint because it did not demonstrate a statistically significant difference in absolute IOP from placebo at every single one of the 12 time points comprising the primary endpoint. This was due to a larger than expected treatment effect in the placebo/vehicle group, as compared to both our prior Phase 2 data and a recent meta-analysis examining placebo responses from 10 placebo-controlled trials, which showed a placebo/vehicle result of -2.01 mmHg (Raber, et al). During analysis of the IOP data from the trial, a treatment-by-site interaction was found where a small number of sites (4 sites out of a total of 55) caused an important change in the expected vehicle results. The review of the MATrX-1 data is ongoing and we expect data from our Phase 2 trial with our FDC product candidate in July 2017. We are also analyzing *trabodenson*’s utility beyond the lowering of eye pressure, including its neuroprotective activity in the back of the eye. Additionally, we are evaluating the potential for selective adenosine mimetics to address optic neuropathies and other degenerative retinal diseases and to improve the patho-physiology associated with dry eye disease. However, there can be no assurance that we will be able to pursue further development or obtain regulatory approval for any indications using *trabodenson*. While we believe these results, along with further exploratory analyses, will be integral in

determining the path forward for our *trabodenoson* monotherapy, there can be no assurance that we will be able to pursue further development efforts or obtain regulatory approval.

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;
- maintenance of existing relationships and 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 and efficacy 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*. The results of our chronic toxicology program could identify a safety problem, or potential pivotal trials of *trabodenoson* monotherapy or our current Phase 2 program for the FDC product candidate could fail to demonstrate efficacy in lowering IOP, especially in light of our Phase 3 results, or could identify safety issues related to *trabodenoson*, which would materially and adversely affect our development strategy. Given the complexity of the design and multiple arms of our current and on-going Phase 2 trial with our FDC product candidate, with each arm having a modest number of patients who will have been on an IOP-lowering medication, it may be difficult to demonstrate a clear treatment effect.

***Our MATrX-1 pivotal Phase 3 trial of trabodenoson for the treatment of primary open-angle glaucoma or ocular hypertension did not meet the primary endpoint, which could continue to harm our business and further disappoint our stockholders and cause the trading price of our common stock to continue to decrease.***

Our lead product candidate in development is *trabodenoson* for the treatment of primary open-angle glaucoma or ocular hypertension. In January 2017, we announced top-line data from our MATrX-1 pivotal Phase 3 clinical trial, which failed to meet its primary endpoint. Currently, management in conjunction with its clinical and regulatory advisors are evaluating the clinical and regulatory pathway forward, although this is subject to ongoing review and evaluation. No assurance can be given that a clinical and regulatory pathway forward will be possible without significantly more capital invested in the Company or will otherwise be successful or possible. Further, no assurance can be given that additional capital would be available or that such capital would be available at acceptable terms.

***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 initiated a pivotal Phase 3 program in the fourth quarter of 2015, which consists of two Phase 3 monotherapy pivotal trials and a long-term safety study. We completed our initial Phase 3 trial and reported top-line data on

January 3, 2017. The primary endpoint of the trial was not met, and we expect data from our Phase 2 dose-ranging trial of a fixed-dose combination (“FDC”) of *trabodendoson* and latanoprost in July 2017. We are also analyzing *trabodendoson*’s utility beyond the lowering of eye pressure, including its neuroprotective activity in the back of the eye. Additionally, we are evaluating the potential for selective adenosine mimetics to address optic neuropathies and other degenerative retinal diseases and to improve the patho-physiology associated with dry eye disease. However, there can be no assurance that we will be able to pursue further development or obtain regulatory approval for any indications using *trabodendoson*. We cannot predict whether any of our potential future trials will be successful or whether regulators will agree with our conclusions regarding the preclinical studies and clinical trials we have conducted to date or will conduct. Moreover, any determination of changes in a study design and its confirmation with the FDA could result in a significant range of costs for the Phase 3 pivotal and long-term safety 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 reviewed by the FDA or, if accepted and reviewed, will be approved.

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 or additional risks. 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.

***We are reevaluating our clinical and regulatory pathway forward for our trabodendoson monotherapy product candidate, and our product candidate might not be approved by regulatory authorities or introduced commercially for at least several years, if at all.***

In January 2017, we announced disappointing top-line data from our MATrX-1 pivotal Phase 3 clinical trial, which failed to meet its primary endpoint. Currently, management in conjunction with its clinical and regulatory advisors are evaluating the clinical and regulatory pathway forward based on the data from the MATrX-1 trial. Going forward, *trabodendoson* will require further development and clinical testing and investment prior to obtaining required regulatory approvals, if ever, and commercialization in the United States and abroad. We cannot provide assurance that a new clinical and regulatory pathway will be successful or possible or that *trabodendoson* will be developed successfully or that we will continue development of *trabodendoson* monotherapy. Even if a viable clinical and regulatory pathway forward is identified, we cannot provide assurance that *trabodendoson* will:

- prove to be safe and effective in clinical studies;
- meet applicable regulatory standards or obtain required regulatory approvals;

- demonstrate substantial protective or therapeutic benefits in the prevention or treatment of any disease;
- be capable of being produced in commercial quantities at reasonable costs;
- obtain coverage and favorable reimbursement rates from insurers and other third-party payors; or
- be marketed successfully or achieve market acceptance by physicians and patients.

***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. 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 and may not be successful. 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 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;
- 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 trial 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;
- 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 successfully formulated our fixed-dose combination product candidate in a way that is suitable for Phase 2 clinical use. However, we have not successfully manufactured the product at commercial scale, nor completed stability testing to confirm its acceptability for 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 completed a Phase 2 trial and are currently conducting an additional Phase 2 trial to evaluate the efficacy, tolerability and safety of *trabodenoson* when co-administered with commercially-available *latanoprost* eye drops. We have formulated our FDC product candidate to include these two drugs in a single eye drop. However, we may never be able to formulate or manufacture our FDC product candidate at commercial scale, or be able to demonstrate that the product is stable enough to commercialize. 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 but not limited to 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. We have exposed more than 500 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 recently completed Phase 3 did not produce the results that we expected, and potential future Phase 3 pivotal trials and long-term safety studies of *trabodenoson* monotherapy may not produce the results that we expect or desire.

Our current and planned clinical trials are also designed to test the use of *trabodenoson* in combination with *latanoprost* in a single dosage form. 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 including our Phase 2 trial with our FDC product candidate may produce negative or inconclusive results or may not achieve their primary endpoints, and we may decide, or regulators may require us, to conduct additional clinical trials or implement a clinical hold or cease development;
- 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;
- regulatory authorities may impose a REMS;

- 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 current and 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 *trabodenson* 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, *trabodendoson* 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.

***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.

***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.

***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 *trabodenson* and seek to develop and commercialize a portfolio of new ophthalmic drugs or explore non-ophthalmic opportunities 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 *trabodenson* or that apply *trabodenson* 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 or product candidates 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 product candidates 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.

***If we reallocate our resources to acquire or develop one or more new product candidates, we may not be successful in developing such new product candidates and we will once again be subject to all the risks and uncertainties associated with research and development of products and technologies.***

We have explored the possibility of reallocating our resources toward developing, acquiring, by acquisition or in-license, new product candidates. If we decide to acquire one or more new product candidates, we cannot guarantee that any such acquisition would result in the identification and successful development of one or more approved and commercially viable products. The development of products and technologies is subject to a number of risks and uncertainties, including:

- the time, costs and uncertainty associated with the clinical testing required to demonstrate the safety and effectiveness of a product candidate to obtain regulatory approvals;
- the ability to raise sufficient funds to fund the research and development of any one or more new product candidates;
- the ability to find third party strategic partners to assist or share in the costs of product development, and potential dependence on such strategic partners, to the extent Inotek may rely on strategic partners for future sales, marketing or distribution;
- the ability to protect the intellectual property rights associated with any one or more new product candidates;
- litigation;
- competition;
- ability to comply with ongoing regulatory requirements;
- government restrictions on the pricing and profitability of products in the United States and elsewhere; and
- the extent to which third-party payers, including government agencies, private health care insurers and other health care payers, such as health maintenance organizations, and self-insured employee plans, will cover and pay for newly approved therapies.

#### **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 currently have only one supplier of active pharmaceutical ingredient. 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. The *trabodenoson* polymorph US patent is scheduled to expire in 2033. See "Business—Intellectual Property" included in our Annual Report on Form 10-K for the year ended December 31, 2016, 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 *trabodenson* 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 March 31, 2017, 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 in our Annual Report on Form 10-K for the fiscal year ended December 31, 2016 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. The *trabodenoson* polymorph US patent is scheduled to expire in 2033.

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 *trabodenson* 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 nineteen full-time employees as of May 1, 2017, and we outsource to consultants or other organizations a portion of our operations, including but not limited to research and development and conduct of clinical trials and certain administrative functions. In order to commercialize our product candidates, we will need to substantially increase our operations. We expect to significantly expand our employment base when and if 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. 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. 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.

***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. If we market any products, 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, 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 or mergers 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 companies, businesses, technologies, services, products or other product candidates or merge with other companies in the future that we believe are a strategic fit with our business. We have no present agreement regarding any material acquisitions or other transactions. However, if we do undertake any acquisitions or mergers, the process of integrating an acquired or merged 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 acquired or merged companies, which may reduce the value of the acquisition or merger, or give rise to additional integration costs. Future acquisitions or mergers could result in additional issuances of equity securities that would dilute the ownership of existing stockholders. Future acquisitions or mergers 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 or merger.

***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 covers 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 or product candidates 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 product candidates 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 or product candidate 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.

***A breach of the Company's computer systems and networks could materially adversely affect the Company's business and financial condition.***

Our business requires us, including some of our vendors, to use and store personally identifiable and other sensitive information, such as health and medical data, for employees and patients. The security measures put in place by the Company, and such vendors, cannot provide absolute security, and the Company and our vendors' information technology infrastructure may be vulnerable to criminal cyber-attacks or data security incidents due to employee error, malfeasance, or other vulnerabilities. The techniques used by criminals to obtain unauthorized access to sensitive data are increasing in sophistication and are often novel, or change frequently. Such attacks now often take the form of phishing, spear-phishing, and other forms of human engineering and impersonation. These attacks could target not only personally identifiable information of the Company's employees and patients but the Company's intellectual property, trade secrets (such as drug formulations), and other proprietary information. The Company may be unable to anticipate these techniques or implement adequate preventative measures. As a result, there is no guarantee that despite the Company's best efforts, the Company will not become the victim of such an attack in the future, that unauthorized parties will not gain access to sensitive data stored on the Company's systems or the systems of Company's vendors, or that any such incident will be discovered in a timely manner.

Any such incident could compromise the Company's or such vendors' networks, and the information stored by the Company or such vendors could be accessed, misused, shared publicly, corrupted, lost, held for ransom, or stolen, resulting in fraud, including wire fraud related to Company assets, corporate espionage, or other harm. Moreover, if a data security incident or breach affects the Company's systems or such vendors' systems or results in the unauthorized release of personally identifiable information, the Company's reputation could be materially harmed and the Company may be exposed to a risk of loss or litigation and possible liability, which could result in a material adverse effect on the Company's business, results of operations, and financial condition. In the event clinical or other medical data from patients enrolled in clinical trials is exposed to unauthorized persons, either by the Company or the Company's vendors, the Company could face challenges enrolling patients in future trials. The Company's insurance coverage may not cover or may be inadequate to cover the losses it could incur should the Company experience a major data security event.

***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.

## **Risks Related to Ownership of Our Common Stock**

***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.

***If we fail to maintain the listing of our common stock with a U.S. national securities exchange, the liquidity of our common stock could be adversely affected.***

If our common stock is delisted by NASDAQ, our common stock may be eligible to trade on the OTC Bulletin Board or another over-the-counter market. Any such alternative would likely result in it being more difficult for us to raise additional capital through the public or private sale of equity securities and for investors to dispose of, or obtain accurate quotations as to the market value of, our common stock. In addition, there can be no assurance that our common stock would be eligible for trading on any such alternative exchange or markets.

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

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. Our common stock is listed on NASDAQ. Since shares of our common stock were sold in our initial public offering in February 2015 at \$6.00 per share, our stock price has reached a high of \$19.45 per share and a low of \$1.50 per share through May 1, 2017.

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. In fact, following our announcement of the results of our Phase 3 monotherapy clinical trial on January 3, 2017, the price of our common stock dropped \$4.35 per share, or 71%, from \$6.10 per share as of the close of business on December 30, 2016, to \$1.75 per share as of the close of business on January 3, 2017. The closing price of our common stock was \$2.00 on April 28, 2017. The following factors, in addition to other factors described in this “Risk Factors” section and elsewhere in our Annual Report on Form 10-K for the fiscal year ended December 31, 2016 and this Quarterly Report on Form 10-Q, 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;
- 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 and our management are parties to a lawsuit which, if adversely decided against, could adversely affect our business and cause the price of our common stock to continue to decrease. We may also be subject to other securities litigation in the future, 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. This risk is especially relevant for us because our stock price declined following our announcement of top-line data from our Phase 3 clinical trial of *trabodenason* for the treatment of primary open-angle glaucoma or ocular hypertension. On January 6, 2017, a purported stockholder of the Company filed a putative class action in the U.S. District Court for the District of Massachusetts, against the Company, David Southwell, Rudolf Baumgartner, Dale Ritter, and William McVicar, captioned *Whitehead v. Inotek Pharmaceuticals Corporation, et al.*, No. 1:17-cv-10025. The complaint alleges violations of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and SEC Rule 10b-5 based on allegedly false and misleading statements and omissions regarding our MATrX-1 Phase 3 clinical trial of *trabodenason*. The lawsuit seeks among other things, unspecified compensatory damages, interest, attorneys' fees and costs, and unspecified equitable/injunctive relief. The Company will vigorously defend plaintiff's claims on the factual record, which it believes will prove that the Company is not liable to the plaintiff in any regard. This litigation or 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 this or future 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 April 14, 2017, our officers and directors, and stockholders who individually own more than 5% of our outstanding common stock, in the aggregate, beneficially owned approximately 57% 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 or noteholders. 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 a stockholder or noteholder, and they may act in a manner that advances their best interests and not necessarily those of other stockholders or noteholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock and 2021 Convertible Notes.



***A substantial number of shares of our common stock are eligible for future sale in the public market, and the issuance or sale of equity, convertible or exchangeable securities in the market, including shares issuable upon conversion of our convertible notes, or the perception of such future sales or issuances, could lead to a decline in the trading price of our common stock.***

Any issuance of shares of our common stock or other securities, including for the purposes of raising capital to fund our operations, financing acquisitions and the expansion of our business, will have a dilutive effect on our existing stockholders. In addition, the perceived market risk associated with the possible issuance of a large number of shares of our common stock, including pursuant to the exercise of our currently outstanding stock options, or issuances of securities convertible or exchangeable into a large number of shares of our common stock could cause some of our stockholders to sell their common stock, thus causing the trading price of our common stock to decline. Subsequent sales of our common stock in the open market, exercises of our currently outstanding stock options and the subsequent sale of the shares acquired thereunder or the sale by us of shares of our common stock or securities convertible or exchangeable into our common stock for capital raising purposes could also have an adverse effect on the trading price of our common stock. If our common stock price declines, it will be more difficult for us to raise additional capital or we may be unable to raise additional capital at all.

In August 2016, we issued \$52.0 million aggregate principal amount of our 5.75% Convertible Senior Notes due 2021 (the “2021 Convertible Notes”). The 2021 Convertible Notes are convertible at the option of the holder at an initial conversion rate of approximately 124.7505 shares of our common stock per \$1,000 principal amount of 2021 Convertible Notes, which is equivalent to an initial conversion price of approximately \$8.02 per share of our common stock, and is subject to adjustment upon certain events and conditions, including the issuance of stock dividends and payment of cash dividends. In addition, in certain circumstances, the conversion rate will also be increased with respect to a holder’s conversion of 2021 Convertible Notes in connection with the occurrence of one or more corporate events. A substantial number of shares of our common stock are reserved for issuance upon conversion of the 2021 Convertible Notes. The issuance of shares of our common stock upon conversion of the 2021 Convertible Notes would dilute the ownership interest of our common stockholders and may materially adversely affect the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities.

In April 2016, we entered into a sales agreement with Cowen and Company, LLC to sell shares of our common stock up to a maximum aggregate offering price of \$50.0 million, from time to time, through an “at the market” equity offering program under which Cowen acts as sales agent (the “ATM”). We did not sell any shares of common stock pursuant to the ATM during the three months ended March 31, 2017. At March 31, 2017, \$45.6 million was available for sale of common stock under the ATM.

In connection with other collaborations, joint ventures, license agreements or future financings that we may enter into in the future, we may issue additional shares of common stock or other equity securities, and the value of the securities issued may be substantial and create additional dilution to our existing and future common 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 holders of our common stock 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, 2016 we had federal and state net operating losses of approximately \$105.3 million and \$62.7 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. 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. We have determined that we have experienced prior ownership changes occurring in 2005, 2007, and 2015. NOLs generated prior to these changes, although subject to an annual limitation, can be utilized in future years as well as any post change 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, 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 SEC 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 \$1.07 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 document, Delaware law and the indenture that governs our 2021 Convertible Notes 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.

In addition, the terms of our 2021 Convertible Notes require us to repurchase the 2021 Convertible Notes in cash in the event of a fundamental change. A takeover of our company, if such takeover constituted a “fundamental change,” would trigger an option of the holders of the 2021 Convertible Notes to require us to repurchase the 2021 Convertible Notes. This may have the effect of delaying or preventing a takeover of our company that would otherwise be beneficial to investors in the 2021 Convertible Notes.

**Item 2. Unregistered Sales of Equity Securities**

None.

**Item 3. Defaults upon Senior Securities**

None.

**Item 4. Mine Safety Disclosures**

Not applicable.

**Item 5. Other Information**

None.

**Item 6. Exhibits**

The exhibits filed as part of this Quarterly Report on Form 10-Q are set forth on the Exhibit Index, which is incorporated herein by reference.

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

INOTEK PHARMACEUTICALS CORPORATION

May 10, 2017

By: /s/ David P. Southwell

David P. Southwell

*President, Chief Executive Officer and Director*

*(Principal Executive Officer)*

May 10, 2017

By: /s/ Dale Ritter

Dale Ritter

*Vice President—Finance*

*(Principal Financial and Accounting Officer)*

**EXHIBIT INDEX**

Exhibit No.	Description	Incorporated by Reference to:			
		Form or Schedule	Exhibit No.	Filing Date with SEC	SEC File Number
3.1	Amended and Restated Certificate of Incorporation of the Registrant.	10-K	3.1	3/31/15	001-36829
3.2	Amended and Restated By-Laws of the Registrant.	10-K	3.2	3/31/15	001-36829
4.1	Specimen Common Stock Certificate of the Registrant.	10-K	4.1	3/31/15	001-36829
4.2	Base Indenture, dated as of August 5, 2016, by and between the Registrant and Wilmington Trust, National Association	8-K	4.1	8/5/2016	001-36829
4.3	First Supplemental Indenture, dated as of August 5, 2016, by and between the Registrant and Wilmington Trust, National Association	8-K	4.2	8/5/2016	001-36829
4.4	Form of 5.75% Convertible Senior Note due 2021	8-K	4.3	8/5/2016	001-36829
31.1*	Certification of Principal Executive Officer pursuant to Exchange Act rules 13a-14 or 15d-14.				
31.2*	Certification of Principal Financial Officer pursuant to Exchange Act rules 13a-14 or 15d-14.				
32.1*	Certification of Principal Executive Officer and Principal Financial Officer pursuant to Exchange Act rules 13a-14(b) or 15d-14(b) and 18 U.S.C. Section 1350.				
101.INS	XBRL Instance Document.				
101.SCH	XBRL Taxonomy Extension Schema Document.				
101.CAL	XBRL Taxonomy Extension Calculation Document.				
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.				
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document.				
101.PRE	XBRL Taxonomy Extension Presentation Link Document.				

\* Filed herewith.

## CERTIFICATIONS

I, David P. Southwell, certify that:

1. I have reviewed this quarterly report on Form 10-Q for the period ended March 31, 2017 of Inotek Pharmaceuticals Corporation;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 10, 2017

/s/ David P. Southwell

David P. Southwell

*President, Chief Executive Officer and Director  
(Principal Executive Officer)*

## CERTIFICATIONS

I, Dale Ritter, certify that:

1. I have reviewed this quarterly report on Form 10-Q for the period ended March 31, 2017 of Inotek Pharmaceuticals Corporation;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 10, 2017

/s/ Dale Ritter

Dale Ritter

*Vice President-Finance*

*(Principal Financial Officer)*



**CERTIFICATION PURSUANT TO  
18 U.S.C. SECTION 1350,  
AS ADOPTED PURSUANT TO  
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the quarterly report on Form 10-Q of Inotek Pharmaceuticals Corporation (the "Company") for the period ended March 31, 2017, as filed with the United States Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers hereby certifies, pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, 18 U.S.C. Section 1350, that to his knowledge:

- 1) the Report which this statement accompanies fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and
- 2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: May 10, 2017

/s/ David P. Southwell

David P. Southwell

*President, Chief Executive Officer and Director  
(Principal Executive Officer)*

Date: May 10, 2017

/s/ Dale Ritter

Dale Ritter

*Vice President-Finance  
(Principal Financial Officer)*