Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended September 30, 2019

Or

o **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: 001-36080

IVERIC bio, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**20-8185347**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
One Penn Plaza, 35th Floor **New York, NY**	**10119**
(Address of principal executive offices)	(Zip Code)

(212) 845-8200
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.001 par value per share	ISEE	The Nasdaq Global Select Market

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 o No

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted 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 such files). ☒ Yes o No

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

Large accelerated filer ☐	Accelerated filer x	Non-accelerated filer ☐	Smaller reporting company x	Emerging growth company ☐

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. o

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

As of November 8, 2019 there were 41,606,189 shares of Common Stock, $0.001 par value per share, outstanding.

TABLE OF CONTENTS

FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Quarterly Report on Form 10-Q, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "goals," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Quarterly Report on Form 10-Q include, among other things, statements about:

- the potential benefits of our business plan and strategy to develop our therapeutic and gene therapy product candidates and programs and pursue our collaborative gene therapy sponsored research programs;
- our expectations regarding the impact of results from our OPH2003 clinical trial evaluating Zimura for the treatment of geographic atrophy secondary to dry age-related macular degeneration on our business strategy, including our plans to pursue further development of Zimura and/or seek potential collaboration or outlicensing opportunities;
- our expectations regarding the potential for Zimura to receive regulatory approval for the treatment of geographic atrophy secondary to dry age-related macular degeneration based on the clinical trial results we have received to date and results from any planned or future clinical trials;
- our expectations related to our use of available cash;
- our estimates regarding expenses, future revenues, capital requirements and needs for, and ability to obtain, additional financing;
- the timing, costs, conduct and outcome of our ongoing and planned research and preclinical development activities, including statements regarding the timing of the initiation of and completion of these activities, and the costs to obtain and timing of receipt of results from such activities, and the impact of the results of such activities on our business strategy;
- the timing, costs, conduct and outcome of our ongoing clinical trials, including statements regarding the timing of the completion of such clinical trials, the costs to obtain and timing of receipt of results from such clinical trials, and the impact of the results of such clinical trials on our business strategy;
- our ability to establish and maintain arrangements and capabilities for the manufacture of our product candidates;
- the timing of and our ability to obtain marketing approval of our product candidates, and the ability of our product candidates to meet existing or future regulatory standards;
- our ability to consummate business development transactions, including for collaboration or out-licensing opportunities for further clinical development and potential commercialization of Zimura or in-license or other opportunities to acquire rights to additional product candidates or technologies to treat retinal diseases;
- the potential advantages of our product candidates and other technologies that we are pursuing, including the advantages and limitations of inhibition of complement C5 and HtrA1, gene therapy, including the use of minigenes, and other mechanisms of action for which we are pursuing development of our product candidates;
- our estimates regarding the potential market opportunity for our product candidates;
- our sales, marketing and distribution capabilities and strategy;
- the rate and degree of potential market acceptance and clinical utility of our product candidates, if approved;
- the potential receipt of revenues from future sales of our product candidates, if approved;
- our intellectual property position;

- the impact of existing and new governmental laws and regulations; and
- our competitive position.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and our stockholders should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Quarterly Report on Form 10-Q, particularly in the "Risk Factors" section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, licenses, dispositions, joint ventures or investments we may make.

You should read this Quarterly Report on Form 10-Q and the documents that we have filed as exhibits to this Quarterly Report on Form 10-Q and our other periodic reports, completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this Quarterly Report on Form 10-Q are made as of the date of this Quarterly Report on Form 10-Q, and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

USE OF TRADEMARKS

The trademarks, trade names and service marks appearing in this Quarterly Report on Form 10-Q are the property of their respective owners. We have omitted the ® and ™ designations, as applicable, for the trademarks named in this Quarterly Report on Form 10-Q after their first reference in this Quarterly Report on Form 10-Q.

PART I—FINANCIAL INFORMATION

Item 1. Financial Statements

IVERIC bio, Inc.
Unaudited Consolidated Balance Sheets
(in thousands, except share and per share data)

	September 30, 2019	December 31, 2018
Assets		
Current assets		
Cash and cash equivalents	$ 94,851	$ 131,201
Prepaid expenses and other current assets	1,110	2,086
Income tax receivable	1,012	—
Total current assets	96,973	133,287
Property and equipment, net	212	335
Right-of-use asset, net	745	—
Income tax receivable, non-current	882	3,529
Other assets	11	14
Total assets	$ 98,823	$ 137,165
Liabilities and Stockholders' Equity		
Current liabilities		
Accrued research and development expenses	$ 4,950	$ 7,337
Accounts payable and accrued expenses	3,666	5,869
Lease liability	745	—
Total current liabilities	9,361	13,206
Total liabilities	9,361	13,206
Stockholders' equity		
Preferred stock—$0.001 par value, 5,000,000 shares authorized, no shares issued or outstanding	$ —	$ —
Common stock—$0.001 par value, 200,000,000 shares authorized, 41,601,639 and 41,397,197 shares issued and outstanding at September 30, 2019 and December 31, 2018, respectively	42	41
Additional paid-in capital	552,468	545,585
Accumulated deficit	(463,048)	(421,667)
Total stockholders' equity	89,462	123,959
Total liabilities and stockholders' equity	$ 98,823	$ 137,165

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

IVERIC bio, Inc.
Unaudited Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except per share data)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Operating expenses:				
Research and development	$ 10,383	$ 9,407	$ 28,077	$ 25,609
General and administrative	4,674	5,968	15,353	17,945
Total operating expenses	15,057	15,375	43,430	43,554
Loss from operations	(15,057)	(15,375)	(43,430)	(43,554)
Interest income	495	637	1,782	1,711
Other income (expense)	—	(1)	151	(17)
Loss before income tax provision (benefit)	(14,562)	(14,739)	(41,497)	(41,860)
Income tax provision (benefit)	(125)	6	(116)	(833)
Net loss	$ (14,437)	$ (14,745)	$ (41,381)	$ (41,027)
Comprehensive loss	$ (14,437)	$ (14,745)	$ (41,381)	$ (41,027)
Net loss per common share:				
Basic and diluted	$ (0.35)	$ (0.41)	$ (1.00)	$ (1.13)
Weighted average common shares outstanding:				
Basic and diluted	41,552	36,202	41,486	36,181

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

IVERIC bio, Inc.

Unaudited Consolidated Statements of Stockholders' Equity

(in thousands)

	Preferred Stock		Common Stock		Additional paid-in capital	Accumulated Deficit	Total
	Shares	Amount	Shares	Amount			
Balance at December 31, 2018	—	$ —	41,397	$ 41	$ 545,585	$ (421,667)	$ 123,959
Issuance of common stock under employee stock compensation plans	—	—	56	—	41	—	41
Share-based compensation	—	—	—	—	2,470	—	2,470
Net loss	—	—	—	—	—	(12,501)	(12,501)
Balance at March 31, 2019	—	$ —	41,453	$ 41	$ 548,096	$ (434,168)	$ 113,969
Issuance of common stock under employee stock compensation plans	—	—	24	—	—	—	—
Share-based compensation	—	—	—	—	2,207	—	2,207
Net loss	—	—	—	—	—	(14,443)	(14,443)
Balance at June 30, 2019	—	$ —	41,477	$ 41	$ 550,303	$ (448,611)	$ 101,733
Issuance of common stock under employee stock compensation plans	—	$ —	50	$ 1	$ 39	$ —	$ 40
Share-based compensation	—	$ —	—	$ —	$ 2,126	$ —	$ 2,126
Issuance of common stock	—	$ —	75	$ —	$ —	$ —	$ —
Net loss	—	$ —	—	$ —	$ —	$ (14,437)	$ (14,437)
Balance at September 30, 2019	—	$ —	41,602	$ 42	$ 552,468	$ (463,048)	$ 89,462

	Preferred Stock		Common Stock		Additional paid-in capital	Accumulated Deficit	Total
	Shares	Amount	Shares	Amount			
Balance at December 31, 2017	—	$ —	36,110	$ 36	$ 522,759	$ (484,754)	$ 38,041
Issuance of common stock under employee stock compensation plans	—	—	54	—	27	—	27
Share-based compensation	—	—	—	—	3,082	—	3,082
Net loss	—	—	—	—	—	(13,073)	(13,073)
Balance at March 31, 2018	—	$ —	36,164	$ 36	$ 525,868	$ (497,827)	$ 28,077
Issuance of common stock under employee stock compensation plans	—	—	24	—	—	—	—
Share-based compensation	—	—	—	—	2,662	—	2,662
Net loss	—	—	—	—	—	(13,209)	(13,209)
Balance at June 30, 2018	—	$ —	36,188	$ 36	$ 528,530	$ (511,036)	$ 17,530
Issuance of common stock under employee stock compensation plans	—	$ —	30	$ —	$ 38	$ —	$ 38
Share-based compensation	—	$ —	—	$ —	$ 2,604	$ —	$ 2,604
Net loss	—	$ —	—	$ —	$ —	$ (14,745)	$ (14,745)
Balance at September 30, 2018	—	$ —	36,218	$ 36	$ 531,172	$ (525,781)	$ 5,427

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

IVERIC bio, Inc.

Unaudited Consolidated Statements of Cash Flows

(in thousands)

	Nine Months Ended September 30,	
	2019	2018
Operating Activities		
Net loss	$ (41,381)	$ (41,027)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation and other expense	123	139
Gain on sale of property and equipment	(150)	—
Deferred income taxes	—	233
Share-based compensation	6,803	8,348
Changes in operating assets and liabilities:		
Income tax receivable	1,635	1,387
Prepaid expense and other assets	979	1,096
Accrued research and development expenses	(2,387)	932
Accounts payable and accrued expenses	(2,203)	(2,937)
Net cash used in operating activities	(36,581)	(31,829)
Investing Activities		
Proceeds from sale of assets	150	—
Net cash provided by (used in) investing activities	150	—
Financing Activities		
Proceeds from employee stock plan purchases	81	65
Net cash provided by financing activities	81	65
Net change in cash and cash equivalents	(36,350)	(31,764)
Cash and cash equivalents		
Beginning of period	131,201	166,972
End of period	$ 94,851	$ 135,208
Supplemental disclosure of cash paid		
Income tax refunds received	$ 1,765	$ 2,467

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

IVERIC bio, Inc.
Notes to Unaudited Consolidated Financial Statements
(in thousands, except per share data)

1. Business

Description of Business and Organization

IVERIC bio, Inc. (the “Company”), formerly Ophthotech Corporation, was incorporated on January 5, 2007, in Delaware. The Company is a science-driven biopharmaceutical company focused on the discovery and development of novel treatment options for retinal diseases with significant unmet medical needs. The Company is currently developing both therapeutic product candidates for age-related retinal diseases and gene therapy product candidates for orphan inherited retinal diseases ("IRDs"). In April 2019, the Company changed its name from Ophthotech Corporation to IVERIC bio, Inc. as the Company continued to broaden its focus to include gene therapies.

The Company recently announced initial, top-line data from its international, randomized, double masked, sham controlled multi-center clinical trial (the "OPH2003 trial"), assessing the safety and efficacy of its most advanced product candidate, Zimura® (avacincaptad pegol), a complement C5 inhibitor, for the treatment of geographic atrophy ("GA"). GA is the advanced stage of dry age-related macular degeneration ("AMD") and is characterized by retinal cell death and degeneration of tissue in the central portion of the retina, or the macula, which may result in loss of vision. The top-line data confirmed that Zimura met the prespecified primary endpoint in the trial in reducing the rate of GA growth in patients with dry AMD. Based on the data the Company has received from the OPH2003 trial to date, the Company has commenced site selection and planning activities for a second pivotal clinical trial for Zimura in GA with the goal of initiating enrollment in this Phase 3 clinical trial during the first quarter of 2020. The Company plans to continue to explore all options for the future development and potential commercialization of Zimura, including potential collaboration and out-licensing opportunities, while it commences Phase 3 activities.

The Company's therapeutics portfolio consists of two ongoing clinical trials evaluating Zimura and its preclinical development program of High temperature requirement A serine peptidase 1 protein ("HtrA1") inhibitors. In addition to the OPH2003 clinical trial of Zimura in GA, which remains ongoing, the Company has an ongoing randomized, double masked, sham controlled clinical trial evaluating Zimura for the treatment of autosomal recessive Stargardt disease (the "OPH2005 trial"). The Company is developing its HtrA1 inhibitor program for GA and potentially other age-related retinal diseases. The Company previously evaluated Zimura in combination with Lucentis® (ranibizumab), an anti-vascular endothelial growth factor ("anti-VEGF") agent for the treatment of wet AMD, for which the Company completed a Phase 2a safety trial (the "OPH2007 trial") during the fourth quarter of 2018.

The Company's gene therapy portfolio consists of several ongoing research and preclinical development programs that use adeno-associated virus ("AAV") for gene delivery. These AAV gene therapy programs are targeting the following orphan IRDs:

- rhodopsin-mediated autosomal dominant retinitis pigmentosa ("RHO-adRP") which is characterized by progressive and severe bilateral loss of vision leading to blindness;
- IRDs associated with mutations in the *BEST1* gene, including Best vitelliform macular dystrophy, or Best disease, which is generally characterized by bilateral egg yolk-like lesions in the macula, which, over time, progress to atrophy and loss of vision;
- Leber congenital amaurosis type 10 ("LCA10") which is characterized by severe bilateral loss of vision at or soon after birth;
- autosomal recessive Stargardt disease ("STGD1") which is characterized by progressive damage to the macula and retina of young adults, leading to loss of vision; and
- IRDs associated with mutations in the USH2A gene, which include Usher syndrome type 2A and USH2A-associated nonsyndromatic autosomal recessive retinitis pigmentosa.

The Company's business development efforts have resulted in the expansion of its research and development pipeline and the transition of the Company to include a focus on gene therapy. The Company initiated multiple gene therapy sponsored research programs with the University of Massachusetts Medical School ("UMMS") in February 2018 and initiated an additional gene therapy sponsored research program with UMMS for *USH2A*-related IRDs in July 2019. Additionally, the Company in-licensed its novel AAV gene therapy product candidate for the treatment of RHO-adRP ("IC-100") from the University of Florida Research Foundation ("UFRF") and the University of Pennsylvania ("Penn") in June 2018, in-licensed its

novel AAV gene therapy product candidate for the treatment of *BEST1*-related IRDs, including Best disease ("IC-200") from Penn and UFRF in April 2019 and in-licensed its minigene sponsored research program for LCA10 (the "miniCEP290 program") from the University of Massachusetts in July 2019. The Company also acquired its HtrA1 inhibitor program through the acquisition of Inception 4, Inc. ("Inception 4") in October 2018.

2. Summary of Significant Accounting Policies

The Company's significant accounting policies are described in Note 2, "Summary of Significant Accounting Policies," in the notes to the audited consolidated financial statements included in the Company's Annual Report on Form 10-K for the year ended December 31, 2018 filed with the Securities and Exchange Commission ("SEC") on February 28, 2019.

Basis of Presentation

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("GAAP") and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented. The consolidated financial statements include the accounts of the Company and its subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Segment and geographic information

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 and reporting segment.

Use of Estimates

The preparation of financial statements and related disclosures in conformity with GAAP requires management to make estimates and judgments that affect the amounts reported in the financial statements and accompanying notes. The Company bases its estimates and judgments on historical experience and on various other assumptions that it believes are reasonable under the circumstances. The amounts of assets and liabilities reported in the Company's Consolidated Balance Sheets and the amount of expenses reported for each of the periods presented are affected by estimates and assumptions, which are used for, but not limited to, accounting for research and development costs, revenue recognition, accounting for share-based compensation and accounting for income taxes. Actual results could differ from those estimates.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of 90 days or less when purchased to be cash equivalents. The carrying amounts reported in the Balance Sheets for cash and cash equivalents are valued at cost, which approximates their fair value.

As of September 30, 2019, the Company had cash and cash equivalents of approximately $94.9 million.

Concentration of Credit Risk

The Company's financial instruments that are exposed to concentration of credit risk consist primarily of cash and cash equivalents. The Company maintains its cash in bank accounts, the balances of which generally exceed federally insured limits. The Company maintains its cash equivalents in investments in money market funds and, at times, in U.S. Treasury securities and investment-grade corporate debt securities with original maturities of 90 days or less.

Concentration of Suppliers

The Company currently relies exclusively upon a single third-party manufacturer to provide supplies of the drug substance for Zimura on a purchase order basis. The Company also engages a single third-party manufacturer to provide fill/finish services for clinical supplies of Zimura. In addition, the Company currently relies upon a single third-party supplier to supply it with the polyethylene glycol reagent used to manufacture Zimura on a purchase order basis. Furthermore, the Company and its contract manufacturers currently rely upon sole-source suppliers of certain raw materials and other specialized components of production used in the manufacture and fill/finish of Zimura. The Company currently relies exclusively upon a single third-party contract manufacturer for IC-100 and IC-200, and sole-source suppliers for certain starting materials to be used in the manufacture of such product candidates. The Company currently relies upon a single third-party contract manufacturer to produce small quantities of the active pharmaceutical ingredient ("API") for its HtrA1 inhibitors for preclinical development purposes and expects to rely on a single third-party contract manufacturer to conduct process development, scale-up and Good Manufacturing Practices ("GMP") manufacture of the API of its HtrA1 inhibitors for potential preclinical toxicology studies and clinical trials. If the Company's third-party manufacturers or fill/finish service providers should become

unavailable to the Company for any reason, including as a result of capacity constraints, financial difficulties or insolvency, the Company believes that there are a limited number of potential replacement manufacturers, and the Company likely would incur added costs and delays in identifying or qualifying such replacements.

Foreign Currency Translation

The Company considers the U.S. dollar to be its functional currency. Expenses denominated in foreign currencies are translated at the exchange rate on the date the expense is incurred. The effect of exchange rate fluctuations on translating foreign currency assets and liabilities into U.S. dollars is included in the Consolidated Statements of Operations and Comprehensive Loss. Foreign exchange transaction gains and losses are included in the results of operations and are not material in the Company's financial statements.

Financial Instruments

Cash equivalents and available for sale securities are reflected in the accompanying financial statements at fair value. The carrying amount of accounts payable and accrued expenses, including accrued research and development expenses, approximates fair value due to the short-term nature of those instruments.

Leases

The Company has leased its office space and has entered into various other agreements in conducting its business. At inception, the Company determines whether an agreement represents a lease and at commencement evaluates each lease agreement to determine whether the lease is an operating or financing lease. Some of the Company's lease agreements have contained renewal options, tenant improvement allowances, rent holidays and rent escalation clauses, although its remaining outstanding lease for its principal offices has no further options, allowances, holidays or clauses. As described below under "Recently Adopted Accounting Pronouncements," the Company adopted the Financial Accounting Standards Board (“FASB”) Accounting Standards Update (“ASU”) 2016-02, *Leases (Topic 842)* as of January 1, 2019.

Pursuant to ASU 2016-02, all of the Company's leases outstanding on January 1, 2019 continued to be classified as operating leases. With the adoption of ASU 2016-02, the Company recorded an operating lease right-of-use asset and an operating lease liability on its Consolidated Balance Sheet. Right-of-use lease assets represent the Company's right to use the underlying asset for the lease term and the lease obligation represents the Company's commitment to make the lease payments arising from the lease. Right-of-use lease assets and obligations are recognized at the commencement date based on the present value of remaining lease payments over the lease term. As the Company’s leases do not provide an implicit discount rate, the Company has used an estimated incremental borrowing rate based on the information available at the commencement date in determining the present value of lease payments. The right-of-use lease asset includes any lease payments made prior to commencement and excludes any lease incentives. The lease term may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. Operating lease expense is recognized on a straight-line basis over the lease term, subject to any changes in the lease or expectations regarding the terms. Variable lease costs such as common area costs and property taxes are expensed as incurred. For all office lease agreements the Company combines lease and nonlease components. Leases with an initial term of 12 months or less are not recorded on the Company's Consolidated Balance Sheet.

Prior to the adoption of ASU 2016-02, when the Company's lease agreements contained renewal options, tenant improvement allowances, rent holidays and rent escalation clauses, the Company recorded a deferred rent asset or liability equal to the difference between the rent expense and the future minimum lease payments due. The lease expense related to operating leases was recognized on a straight-line basis in the Company's Consolidated Statements of Operations over the term of each lease. In cases where the lessor granted the Company leasehold improvement allowances that reduced the Company's lease expense, the Company capitalized the improvements as incurred and recognized deferred rent, which was amortized over the shorter of the lease term or the expected useful life of the improvements.

Property and Equipment

Property and equipment, which consists mainly of clinical equipment, computers, software, other office equipment, and leasehold improvements, are carried at cost less accumulated depreciation. Depreciation is computed over the estimated useful lives of the respective assets, generally three to ten years, using the straight-line method. Amortization of leasehold improvements is recorded over the shorter of the lease term or estimated useful life of the related asset.

Research and Development

The Company's research and development expenses primarily consist of costs associated with the manufacturing, development and preclinical and clinical testing of its product candidates and costs associated with its collaborative gene

therapy sponsored research programs. The Company's research and development expenses consist of:

- external research and development expenses incurred under arrangements with third parties, such as academic research collaborators, contract research organizations ("CROs"), and contract development and manufacturing organizations ("CDMOs") and other vendors for the production and analysis of drug substance and drug product; and

- employee-related expenses for employees dedicated to research and development activities, including salaries, benefits and share-based compensation expense.

Research and development expenses also include costs of acquired product licenses, in-process research and development, and related technology rights where there is no alternative future use, costs of prototypes used in research and development, consultant fees and amounts paid to collaborators.

All research and development expenses are charged to operations as incurred in accordance with ASC 730, *Research and Development*.

Income Taxes

The Company utilizes the liability method of accounting for deferred income taxes, as set forth in ASC 740, *Income Taxes.* Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the carrying amounts and the tax basis of assets and liabilities. A valuation allowance is established against deferred tax assets when, based on the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. The Company's policy is to record interest and penalties on uncertain tax positions as income tax expense.

Share-Based Compensation

The Company follows the provisions of ASC 718, *Compensation—Stock Compensation*, which requires the measurement and recognition of compensation expense for all share-based payment awards made to employees, non-employee directors and consultants, including employee stock options, restricted stock units (“RSUs”) and options granted to employees to purchase shares under the 2016 Employee Stock Purchase Plan (the “ESPP”). Share-based compensation expense is based on the grant date fair value estimated in accordance with the provisions of ASC 718 and is generally recognized as an expense over the requisite service period, net of estimated forfeitures. For grants containing performance-based vesting provisions, expense is recognized over the estimated achievement period only when the performance-based milestone is deemed probable of achievement. If performance-based milestones are later determined not to be probable of achievement, then all previously recorded stock-based compensation expense associated with such options will be reversed during the period in which the Company makes this determination.

Prior to January 1, 2019, share-based compensation awarded to non-employees was subject to revaluation over the vesting term of each award. Subsequent to the adoption of ASU 2018-07, *Improvements to Non-Employee Share-Based Payment Accounting*, the value of non-employee share-based compensation is measured on the date of grant, similar to share-based compensation granted to employees.

Stock Options

The Company estimates the fair value of stock options granted to employees, non-employee directors and consultants on the date of grant using the Black-Scholes option-pricing model. Due to the lack of trading history, the Company's computation of stock-price volatility is based on the volatility rates of comparable publicly held companies over a period equal to the expected term of the options granted by the Company. The Company's computation of expected term is determined using the "simplified" method, which is the midpoint between the vesting date and the end of the contractual term. The Company believes that it does not have sufficient reliable exercise data in order to justify the use of a method other than the "simplified" method of estimating the expected exercise term of employee stock option grants. The Company utilizes a dividend yield of zero based on the fact that the Company has never paid cash dividends to stockholders and has no current intentions to pay cash dividends. The risk-free interest rate is based on the zero-coupon U.S. Treasury yield at the date of grant for a term equivalent to the expected term of the option.

The weighted-average assumptions used to estimate grant date fair value of stock options using the Black-Scholes option pricing model were as follows for the three and nine months ended September 30, 2019 and 2018:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Expected common stock price volatility	89%	84%	88%	83%
Risk-free interest rate	1.38%-1.84%	2.80%-2.90%	1.38%-2.54%	2.39%-2.90%
Expected term of options (years)	6.1	6.1	5.7	5.8
Expected dividend yield	—	—	—	—

RSUs

The Company estimates the fair value of RSUs granted to employees using the closing market price of the Company's common stock on the date of grant.

ESPP

In April 2016, the Company's board of directors adopted the ESPP pursuant to which the Company may sell up to an aggregate of 1,000,000 shares of its common stock. The ESPP was approved by the Company's stockholders in June 2016. The ESPP is considered compensatory and the fair value of the discount and look back provision are estimated using the Black-Scholes option-pricing model and recognized over the six month withholding period prior to purchase.

Recently Adopted Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-2, *Leases (Topic 842)*. Under the new guidance, lessees will be required to recognize the following for all leases (with the exception of short-term leases) at the commencement date: (1) a lease liability, which is a lessee's obligation to make lease payments arising from a lease, measured on a discounted basis; and (2) a right-of-use asset, which is an asset that represents the lessee's right to use, or control the use of, a specified asset for the lease term. Under the new guidance, lessor accounting is largely unchanged. Certain targeted improvements were made to align, where necessary, lessor accounting with the lessee accounting model and Topic 606, *Revenue from Contracts with Customers*. The new lease guidance simplified the accounting for sale and leaseback transactions primarily because lessees must recognize lease assets and lease liabilities. Lessees will no longer be provided with a source of off-balance sheet financing. Publicly-traded business entities were required to apply the amendments in ASU 2016-2 for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years (i.e., January 1, 2019, for a calendar year entity). Early application was permitted for all publicly-traded business entities and all nonpublicly-traded business entities upon issuance. Lessees (for capital and operating leases) and lessors (for sales-type, direct financing, and operating leases) must apply a modified retrospective transition approach for leases existing at, or entered into after, the beginning of the earliest comparative period presented in the financial statements. The modified retrospective approach does not require any transition accounting for leases that expired before the earliest comparative period presented. Lessees and lessors may not apply a full retrospective transition approach. On January 1, 2019 the Company adopted this guidance utilizing the simplified transition option that allows companies to initially apply the new lease standard at the adoption date and recognize a cumulative-effect adjustment to the opening balance of retained earnings in the period of adoption. The Company elected to adopt the package of practical expedients permitted in Accounting Standards Codification Topic 842, or ASC 842. Accordingly, the Company continues to account for its existing operating leases as operating leases under the new guidance, without reassessing whether the contracts contain a lease under ASC 842 or whether classification of the operating leases would be different under ASC Topic 842.

As a result of the adoption, the Company recognized, as of the beginning of the period of adoption, right-of-use assets and lease liabilities of approximately $1.5 million, which represents the present value of its remaining lease payments using a weighted average estimated incremental borrowing rate of 6%, on its Consolidated Balance Sheet. The adoption of this standard did not have a material impact on the Company's results of operations for the period ended September 30, 2019.

In June 2018, the FASB issued ASU No. 2018-07, *Improvements to Nonemployee Share-Based Payment Accounting*, which supersedes ASC 505-50 and expands the scope of ASC 718 to include all share-based payments arrangements related to the acquisition of goods and services from both employees and nonemployees. For public companies, the amendments became effective for annual reporting periods beginning after December 15, 2018, including interim periods within those annual periods. During the three months ended March 31, 2019, the Company adopted this guidance. The adoption did not have a material impact on its financial statements for the period ended and as of September 30, 2019.

Recent Accounting Pronouncements

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820)*, which modifies the disclosure requirements on fair value measurements in Topic 820, Fair Value Measurement, including, among other changes, the

consideration of costs and benefits when evaluating disclosure requirements. For public companies, the amendments are effective for annual reporting periods beginning after December 15, 2019, including interim periods within those annual periods. Early adoption is permitted. The Company does not expect the adoption of this new accounting guidance to have a material impact on its financial statements or disclosures.

In August 2018, the FASB issued ASU No. 2018-15, *Intangibles - Goodwill and Other - Internal-Use Software* (Subtopic 350-40): *Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract* (a consensus of the FASB Emerging Issues Task Force). ASU 2018-15 aligns the requirements for capitalizing implementation costs incurred in a hosting arrangement that is a service contract with the requirements for capitalizing implementation costs incurred to develop or obtain internal-use software (and hosting arrangements that include an internal-use software license). This guidance is effective for fiscal years beginning after December 15, 2019, and for interim periods within those fiscal years, with early adoption permitted. The Company does not expect the adoption of this new accounting guidance to have a material impact on its financial statements or disclosures.

In November 2018, the FASB issued ASU No. 2018-18, *Collaborative Arrangements (Topic 808)*, which clarifies the interaction between the guidance for collaborative arrangements (Topic 808) and the new revenue recognition standard (Topic 606). For public companies, the amendments are effective for annual reporting periods beginning after December 15, 2019, including interim periods within those annual periods. Early adoption is permitted. The Company does not expect the adoption of this new accounting guidance to have a material impact on its financial statements or disclosures.

3. Net Loss Per Common Share

Basic and diluted net loss per common share is determined by dividing net loss by the weighted average common shares outstanding during the period. For the periods where there is a net loss, shares underlying stock options and RSUs have been excluded from the calculation of diluted net loss per common share because the effect of including such shares would be anti-dilutive. Therefore, the weighted average common shares used to calculate both basic and diluted net loss per common share would be the same. The following table sets forth the computation of basic and diluted net loss per common share for the periods indicated:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Basic and diluted net loss per common share calculation:				
Net loss	$ (14,437)	$ (14,745)	$ (41,381)	$ (41,027)
Weighted average common shares outstanding - basic and dilutive	41,552	36,202	41,486	36,181
Net loss per share of common stock - basic and diluted	$ (0.35)	$ (0.41)	$ (1.00)	$ (1.13)

The following potentially dilutive securities have been excluded from the computations of diluted weighted average common shares outstanding for the periods presented, as the effect of including such shares would be anti-dilutive:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Stock options outstanding	5,468	4,855	5,468	4,855
Restricted stock units	695	184	695	184
Total	6,163	5,039	6,163	5,039

4. Cash, Cash Equivalents and Available for Sale Securities

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at the date of purchase to be cash equivalents. As of September 30, 2019 and December 31, 2018, the Company had cash and cash equivalents of approximately $94.9 million and $131.2 million, respectively. Cash and cash equivalents included cash of $3.8 million at September 30, 2019 and $4.4 million at December 31, 2018. Cash and cash equivalents at September 30, 2019 and December 31, 2018 included $91.1 million and $126.8 million, respectively, of investments in money market funds and certain investment-grade corporate debt securities with original maturities of 90 days or less.

The Company considers securities with original maturities of greater than 90 days at the date of purchase to be available for sale securities. The Company held no available for sale securities at September 30, 2019 or at December 31, 2018, respectively.

The Company believes that its existing cash and cash equivalents as of September 30, 2019 will be sufficient to fund its operations and capital expenditure requirements as currently planned through the first half of 2021. This estimate is based on the Company's current business plan, including the continuation of its current research and development programs and site selection and planning activities for its Phase 3 clinical trial for Zimura in GA. This estimate does not reflect any additional expenditures, including associated development costs, in the event it in-licenses or acquires any new product candidates or commences any new sponsored research programs. The Company has based this estimate on assumptions that may prove to be wrong, and it could use its available capital resources sooner than it currently expects.

5. Share-Based Compensation

Pursuant to the evergreen provisions of the Company's 2013 stock incentive plan (the "2013 Plan"), annual increases have resulted in the addition of an aggregate of approximately 8,554,000 additional shares to the 2013 Plan, including for 2019, an increase of approximately 1,656,000 shares, or approximately 4% of the total number of shares of the Company's common stock outstanding as of January 1, 2019. As of September 30, 2019, the Company had approximately 2,755,000 shares available for grant under the 2013 Plan.

Share-based compensation expense, net of estimated forfeitures, includes expenses related to stock options and RSUs granted to employees, non-employee directors and consultants, as well as options granted to employees to purchase shares under the ESPP. Stock-based compensation by award type was as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Stock options	$ 1,447	$ 1,827	$ 4,557	$ 5,795
Restricted stock units	667	764	2,197	2,529
Employee stock purchase plan	12	13	49	24
Total	$ 2,126	$ 2,604	$ 6,803	$ 8,348

The Company allocated stock-based compensation expense in the Company’s Consolidated Statements of Operations and Comprehensive Loss as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Research and development	$ 942	$ 1,171	$ 3,101	$ 3,717
General and administrative	1,184	1,433	3,702	4,631
Total	$ 2,126	$ 2,604	$ 6,803	$ 8,348

Stock Options

A summary of the stock option activity, weighted average exercise prices, options outstanding, exercisable and expected to vest as of September 30, 2019 is as follows (in thousands except weighted average exercise price):

	Number of Shares Underlying Options	Weighted Average Exercise Price
Outstanding, December 31, 2018	5,903	$ 13.72
Granted	177	$ 1.31
Forfeited	(420)	$ 19.59
Expired	(192)	$ 26.87
Outstanding, September 30, 2019	5,468	$ 12.41
Vested and exercisable, September 30, 2019	2,946	$ 20.06
Vested and expected to vest, September 30, 2019	5,266	$ 12.76

As of September 30, 2019, there were approximately $4.9 million of unrecognized compensation costs, net of estimated forfeitures, related to stock option awards grants, which are expected to be recognized over a remaining weighted average period of 1.7 years.

RSUs

The following table presents a summary of the Company's outstanding RSU awards granted as of September 30, 2019 (in thousands except weighted average grant-date fair value):

	Restricted Stock Units		Weighted Average Grant-Date Fair Value
Outstanding, December 31, 2018	679	$	15.61
Awarded	102	$	1.26
Vested	(59)	$	52.77
Forfeited	(27)	$	13.77
Outstanding, September 30, 2019	695	$	10.48
Outstanding, Expected to vest	576	$	5.17

As of September 30, 2019, there were approximately $1.5 million of unrecognized compensation costs, net of estimated forfeitures, related to RSUs grants, which are expected to be recognized over a remaining weighted average period of 1.5 years.

ESPP

As of September 30, 2019, there were 881,763 shares available for future purchases under the ESPP. There were 38,944 and 70,466 shares of common stock issued under the ESPP during the three and nine months ended September 30, 2019. Cash proceeds from ESPP purchases were $39 thousand and $81 thousand during the three and nine months ended September 30, 2019. There were 19,184 and 31,413 shares of common stock issued under the ESPP during the three and nine months ended September 30, 2018. Cash proceeds from ESPP purchases were $38 thousand and $65 thousand during the three and nine months ended September 30, 2018.

6. Income Taxes

For the three and nine months ended September 30, 2019, the Company recorded a $0.1 million benefit for income taxes. For the three and nine months ended September 30, 2018, the Company recorded a de minimis provision for income taxes and a $0.8 million benefit for income taxes, respectively. The income tax benefit for the three and nine months ended September 30, 2019 was primarily to reflect a settlement of a local tax audit. The benefit for income taxes recorded during the nine months ended September 30, 2018 includes the settlement of a local tax audit recorded by the Company during the three months ended June 30, 2018 offset partially by the provision for income taxes recorded by the Company during the three months ended March 31, 2018 to reflect the impact of sequestration on the Company's estimate of refundable AMT credits.

The Company will continue to evaluate its ability to realize its deferred tax assets on a quarterly basis and will adjust such amounts in light of changing facts and circumstances including, but not limited to, future projections of taxable income, tax legislation, rulings by relevant tax authorities, the progress of ongoing tax audits and the regulatory approval of products currently under development. Any additional changes to the valuation allowance recorded on deferred tax assets in the future would impact the Company’s income taxes.

7. Fair Value Measurements

ASC 820, *Fair Value Measurements and Disclosures*, defines fair value as the price that would be received to sell an asset, or paid to transfer a liability, in the principal or most advantageous market in an orderly transaction between market participants on the measurement date. The fair value standard also establishes a three-level hierarchy, which requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value.

The Company reviews investments on a periodic basis for other than temporary impairments. This review is subjective as it requires management to evaluate whether an event or change in circumstances has occurred in the period that may have a significant adverse effect on the fair value of the investment. The Company uses the market approach to measure fair value for its financial assets. The market approach uses prices and other relevant information generated by market transactions involving identical or comparable assets. The Company classifies its investment-grade corporate debt securities within the fair value hierarchy as Level 2 assets, as it primarily utilizes quoted market prices or rates for similar instruments to value these securities.

The valuation hierarchy is based upon the transparency of inputs to the valuation of an asset or liability on the measurement date. The three levels are defined as follows:

- Level 1—inputs to the valuation methodology are quoted prices (unadjusted) for an identical asset or liability in an active market. The Company's Level 1 assets consist of investments in money market funds and U.S. Treasury securities.

- Level 2—inputs to the valuation methodology include quoted prices for a similar asset or liability in an active market or model-derived valuations in which all significant inputs are observable for substantially the full term of the asset or liability. The Company's Level 2 assets may consist of investments in investment-grade corporate debt securities.

- Level 3—inputs to the valuation methodology are unobservable and significant to the fair value measurement of the asset or liability. The Company does not hold any assets that are measured using Level 3 inputs.

The following table presents, for each of the fair value hierarchy levels required under ASC 820, the Company's assets and liabilities that are measured at fair value on a recurring basis as of September 30, 2019:

	Fair Value Measurement Using		
	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
Assets			
Investments in money market funds*	$ 83,315	$ —	$ —
Investments in investment-grade corporate debt securities*	$ —	$ 7,779	$ —

The following table presents, for each of the fair value hierarchy levels required under ASC 820, the Company's assets and liabilities that are measured at fair value on a recurring basis as of December 31, 2018:

	Fair Value Measurement Using		
	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
Assets			
Investments in money market funds*	$ 97,402	$ —	$ —
Investments in investment-grade corporate debt securities*	$ —	$ 29,425	$ —

* Investments in money market funds and investment-grade corporate debt securities with maturities less than 90 days are reflected in cash and cash equivalents in the accompanying Consolidated Balance Sheets.

No transfer of assets between Level 1 and Level 2 of the fair value measurement hierarchy occurred during the three and nine months ended September 30, 2019.

The Company held no available for sale securities at September 30, 2019 or at December 31, 2018.

8. Operating Leases

The Company leases office space located in New York, New York and Princeton, New Jersey under non-cancelable operating lease arrangements. The lease for the Company's New York office space expires at the end of June 2020, whereas the sublease for the Company's Princeton office space expires in March 2020. As of January 1, 2019, the Company recognized right-of-use assets and lease liabilities of approximately $1.5 million, which represents the present value of its remaining lease payments using a weighted average estimated incremental borrowing rate of 6%.

For the three and nine months ended September 30, 2019, lease and rent expense was $0.3 million and $0.8 million, respectively. Cash paid from operating cash flows for amounts included in the measurement of lease liabilities was $0.3 million and $0.8 million, respectively, for the three and nine months ended September 30, 2019. At September 30, 2019, the Company's operating leases had a weighted average remaining lease term of 0.7 years.

The following presents the maturity of the Company's operating lease liabilities as of September 30, 2019:

	September 30, 2019
Remainder of 2019	$ 260
2020	504
Total remaining obligation	764
Less imputed interest	(19)
Present value of lease liabilities	$ 745

9. Commitments and Contingencies

Zimura - Archemix Corp.

The Company is party to an agreement with Archemix Corp., or Archemix, under which the Company in-licensed rights in certain patents, patent applications and other intellectual property related to Zimura and pursuant to which the Company may be required to pay sublicense fees and make milestone payments (the "C5 License Agreement"). Under the C5 License Agreement, for each anti-C5 aptamer product that the Company may develop under the agreement, including Zimura, the Company is obligated to make payments to Archemix of up to an aggregate of $57.5 million if the Company achieves specified development, clinical and regulatory milestones, with $30.5 million of such payments relating to a first indication, $24.5 million of such payments relating to second and third indications and $2.5 million of such payments relating to sustained delivery applications. Under the C5 License Agreement, the Company is also obligated to make additional payments to Archemix of up to an aggregate of $22.5 million if the Company achieves specified commercial milestones based on net product sales of all anti-C5 products licensed under the agreement. The Company is also obligated to pay Archemix a double-digit percentage of specified non-royalty payments the Company may receive from any sublicensee of its rights under the C5 License Agreement. The Company is not obligated to pay Archemix a running royalty based on net product sales in connection with the C5 License Agreement.

IC-100 - University of Florida and the University of Pennsylvania

Under its exclusive license agreement with UFRF and Penn for rights to IC-100, the Company is obligated to make payments to UFRF, for the benefit of Penn and UFRF (together, the "Licensors"), of up to an aggregate of $23.5 million if the Company achieves specified clinical, marketing approval and reimbursement approval milestones with respect to a licensed product and up to an aggregate of an additional $70.0 million if the Company achieves specified commercial sales milestones with respect to a licensed product. The Company is also obligated to pay UFRF, for the benefit of the Licensors, a low single-digit percentage of net sales of licensed products. The Company is also obligated to pay UFRF, for the benefit of the Licensors, a double-digit percentage of specified non-royalty payments the Company may receive from any third-party sublicensee of the licensed patent rights. Further, if the Company receives a rare pediatric disease priority review voucher from the U.S. Food and Drug Administration ("FDA") in connection with obtaining marketing approval for a licensed product and the Company subsequently uses such priority review voucher in connection with a different product candidate, the Company will be obligated to pay UFRF, for the benefit of the Licensors, aggregate payments in the low double-digit millions of dollars based on certain approval and commercial sales milestones with respect to such other product candidate. In addition, if the Company sells such a priority review voucher to a third party, the Company will be obligated to pay UFRF, for the benefit of the Licensors, a low double-digit percentage of any consideration received from such third party in connection with such sale.

IC-200 - University of Pennsylvania and the University of Florida

Under its exclusive license agreement with Penn and UFRF for rights to IC-200, the Company is obligated to make payments to Penn, for the benefit of the Licensors, of up to an aggregate of $15.7 million if the Company achieves specified clinical, marketing approval and reimbursement approval milestones with respect to one licensed product and up to an aggregate of an additional $3.1 million if the Company achieves these same milestones with respect to a different licensed product. In addition, the Company is obligated to make payments to Penn, for the benefit of the Licensors, of up to an aggregate of $48.0 million if the Company achieves specified commercial sales milestones with respect to one licensed product and up to an aggregate of an additional $9.6 million if the Company achieves these same milestones with respect to a different licensed product. The Company is also obligated to pay Penn, for the benefit of the Licensors, a low single-digit percentage of net sales of licensed products. The Company is also obligated to pay Penn, for the benefit of the Licensors, a high single-digit to a mid-teen percentage of specified non-royalty payments the Company may receive from any third-party sublicensee of the licensed patent rights, with the applicable percentage based upon the stage of development of the sublicensed product at the time the Company enters into the sublicense. Further, if the Company receives a rare pediatric disease priority review voucher from the FDA in connection with obtaining marketing approval for a licensed product and the Company subsequently uses such priority

review voucher in connection with a different product candidate outside the scope of the agreement, the Company will be obligated to pay Penn, for the benefit of the Licensors, aggregate payments in the low double-digit millions of dollars based on certain approval and commercial sales milestones with respect to such other product candidate. In addition, if the Company sells such a priority review voucher to a third party, the Company will be obligated to pay Penn, for the benefit of the Licensors, a high single-digit percentage of any consideration received from such third party in connection with such sale.

miniCEP290 Program - University of Massachusetts

On July 22, 2019, the Company entered into its exclusive license agreement with the University of Massachusetts ("UMass") for rights to its miniCEP290 program (the "miniCEP290 License Agreement"). Pursuant to the terms of the miniCEP290 License Agreement, the Company paid UMass a $0.4 million upfront license fee and issued to UMass 75,000 shares of the Company's common stock, which were valued at approximately $0.1 million on July 22, 2019.

Under the miniCEP290 License Agreement, the Company is obligated to pay UMass up to an aggregate of $14.75 million in cash and issue up to 75,000 shares of common stock of the Company if the Company achieves specified clinical and regulatory milestones with respect to a licensed product. In addition, the Company is obligated to pay UMass up to an aggregate of $48.0 million if the Company achieves specified commercial sales milestones with respect to a licensed product. The Company is also obligated to pay UMass royalties at a low single-digit percentage of net sales of licensed products. If the Company or any of its affiliates sublicenses any of the licensed patent rights or know-how to a third party, the Company will be obligated to pay UMass a high single-digit to a mid-tens percentage of the consideration received in exchange for such sublicense, with the applicable percentage based upon the stage of development of the licensed products at the time the Company or the applicable affiliate enters into the sublicense. If the Company receives a priority review voucher from the FDA in connection with obtaining marketing approval for a licensed product, and the Company subsequently uses such priority review voucher in connection with a different product candidate outside the scope of the agreement, the Company will be obligated to pay UMass a low-tens percentage of the fair market value of the priority review voucher at the time of approval of such product candidate and a low-twenties percentage of the fair market value of the priority review voucher at the time of achievement of a specified commercial sales milestone for such product candidate. In addition, if the Company sells such a priority review voucher to a third party, the Company will be obligated to pay UMass a low-thirties percentage of any consideration received from such third party in connection with such sale.

HtrA1 Inhibitors - Former Equityholders of Inception 4

Under the agreement and plan of merger pursuant to which the Company acquired Inception 4 (the "Inception 4 Merger Agreement"), the Company is obligated to make payments to the former equityholders of Inception 4 of up to an aggregate of $105 million, subject to the terms and conditions of the Inception 4 Merger Agreement, if the Company achieves certain specified clinical and regulatory milestones with respect to a product candidate from its HtrA1 inhibitor program, with $45 million of such potential payments relating to GA and $60 million of such potential payments relating to wet AMD. Under the Inception 4 Merger Agreement, the Company does not owe any commercial milestones or royalties based on net sales. The future milestone payments will be payable in the form of shares of the Company's common stock, calculated based on the price of its common stock over a five-trading day period preceding the achievement of the relevant milestone, unless and until the issuance of such shares would, together with all other shares issued in connection with the acquisition, exceed an overall maximum limit of approximately 7.2 million shares, which is equal to 19.9% of the number of issued and outstanding shares of the Company's common stock as of the close of business on the business day prior to the closing date of the Inception 4 acquisition, and will be payable in cash thereafter. The Inception 4 Merger Agreement also includes customary indemnification obligations to the former equityholders of Inception 4, including for breaches of the representations and warranties, covenants and agreements of the Company and its subsidiaries (other than Inception 4) in the Inception 4 Merger Agreement.

Employment Contracts

The Company also has letter agreements with certain employees that require the funding of a specific level of payments if certain events, such as a termination of employment in connection with a change in control or termination of employment by the employee for good reason or by the Company without cause, occur.

Contract Service Providers

In addition, in the course of normal business operations, the Company has agreements with contract service providers to assist in the performance of the Company’s research and development and manufacturing activities. Expenditures to CROs and CDMOs represent significant costs in preclinical and clinical development. Subject to required notice periods and the Company’s obligations under binding purchase orders and any cancellation fees that the Company may be obligated to pay, the Company can elect to discontinue the work under these agreements at any time.

Legal Proceedings

On January 11, 2017, a putative class action lawsuit was filed against the Company and certain of its current and former executive officers in the United States District Court for the Southern District of New York, captioned Frank Micholle v. Ophthotech Corporation, et al., No. 1:17-cv-00210. On March 9, 2017, a related putative class action lawsuit was filed against the Company and the same group of its current and former executive officers in the United States District Court for the Southern District of New York, captioned Wasson v. Ophthotech Corporation, et al., No. 1:17-cv-01758. These cases were consolidated on March 13, 2018. On June 4, 2018, the lead plaintiff filed a consolidated amended complaint (the "CAC"). The CAC purports to be brought on behalf of shareholders who purchased the Company's common stock between March 2, 2015 and December 12, 2016. The CAC generally alleges that the Company and certain of its officers violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning the results of the Company's Phase 2b trial and the prospects of the Company's Phase 3 trials for Fovista in combination with anti-VEGF agents for the treatment of wet AMD. The CAC seeks unspecified damages, attorneys' fees, and other costs. The Company and individual defendants filed a motion to dismiss the CAC on July 27, 2018. On September 18, 2019, the court issued an order dismissing some, but not all, of the allegations in the CAC.

On February 7, 2018, a shareholder derivative action was filed against the members of the Company's board of directors in the New York Supreme Court Commercial Division, captioned Cano v. Guyer, et al., No. 650601/2018. The complaint alleges that the defendants breached their fiduciary duties to the Company by adopting a compensation plan that overcompensates the non-employee members of the Company's board of directors relative to boards of directors of companies of comparable market capitalization and size. The complaint also alleges that the defendants were unjustly enriched as a result of the alleged conduct. The complaint purports to seek unspecified damages, on behalf of the Company, attorneys' fees, and other costs, as well as an order directing the Company to reform and improve its corporate governance and internal procedures to comply with applicable laws. The Company filed a motion to dismiss this case on May 14, 2018. On June 4, 2018, the plaintiff filed an amended complaint. On June 25, 2018, the Company filed a renewed motion to dismiss this case. On December 3, 2018, the parties filed a stipulation of settlement that contemplates that the Company will adopt certain compensation-related governance reforms and does not obligate the defendants or the Company to pay any monetary damages. The court approved the settlement at a hearing on March 12, 2019. As part of the settlement, in April 2019 the Company paid $300,000 in fees and costs to plaintiff's counsel. As contemplated by the settlement, the Company's board of directors adopted certain compensation-related governance reforms, including a non-employee director compensation policy, which the Company's stockholders approved on May 15, 2019 at its 2019 annual meeting.

On August 31, 2018, a shareholder derivative action was filed against current and former members of the Company's board of directors and certain current and former officers of the Company in the United States District Court for the Southern District of New York, captioned Luis Pacheco v. David R. Guyer, et al., Case No. 1:18-cv-07999. The complaint, which is based substantially on the facts alleged in the CAC, alleges that the defendants breached their fiduciary duties to the Company and wasted the Company's corporate assets by failing to oversee the Company's business, and also alleges that the defendants were unjustly enriched as a result of the alleged conduct, including through receipt of bonuses, stock options and similar compensation from the Company, and through sales of the Company's stock between March 2, 2015 and December 12, 2016. The complaint purports to seek unspecified damages on the Company's behalf, attorneys' fees, and other costs, as well as an order directing the Company to reform and improve its corporate governance and internal procedures to comply with applicable laws, including submitting certain proposed amendments to the Company's corporate charter, bylaws and corporate governance policies for vote by the Company's stockholders. On December 14, 2018, the Company filed a motion to dismiss the complaint. On September 19, 2019, the court denied the Company's motion to dismiss this complaint. This matter was subsequently referred to a special litigation committee of the Company's board of directors.

On October 16, 2018, the Company's board of directors received a shareholder demand to investigate and commence legal proceedings against certain members of the Company's board of directors. The demand alleges facts that are substantially similar to the facts alleged in the CAC and the Pacheco complaint and asserts claims that are substantially similar to the claims asserted in the Pacheco complaint. On January 30, 2019, the Company's board of directors received a second shareholder demand from a different shareholder to investigate and commence legal proceedings against certain current and former members of the Company's board of directors based on allegations that are substantially similar to the allegations contained in the first demand letter. These shareholder demands have been referred to a demand review committee of the Company's board of directors.

The Company denies any and all allegations of wrongdoing and intends to vigorously defend against these lawsuits. The Company is unable, however, to predict the outcome of these matters at this time. Moreover, any conclusion of these matters in a manner adverse to the Company and for which it incurs substantial costs or damages not covered by the Company's directors' and officers' liability insurance would have a material adverse effect on its financial condition and business. In addition, the litigation could adversely impact the Company's reputation and divert management's attention and resources from

other priorities, including the execution of its business plan and strategies that are important to the Company's ability to grow its business, any of which could have a material adverse effect on the Company's business.

10. Subsequent Event

On October 28, 2019, the Company announced initial, top-line data from its Phase 2b clinical trial evaluating Zimura for the treatment of GA secondary to dry AMD. As a result of this data, under the terms of the C5 License Agreement, the Company is obligated to pay Archemix a milestone payment of $1.0 million during the first quarter of 2020.

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 together with our financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q and the audited financial statements and related notes and management's discussion and analysis of financial condition and results of operations for the year ended December 31, 2018 included in our Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 28, 2019. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties and should be read together with the "Risk Factors" section of this Quarterly Report on Form 10-Q for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a science-driven biopharmaceutical company focused on the discovery and development of novel treatment options for retinal diseases with significant unmet medical needs. We are currently developing both therapeutic product candidates for age-related retinal diseases and gene therapy product candidates for orphan inherited retinal diseases, or IRDs. In April 2019, we changed our name from Ophthotech Corporation to IVERIC bio, Inc. as we continued to broaden the focus of our company to include gene therapies. We believe that both therapeutics and gene therapy serve an important role in drug development and providing potential treatment options for patients suffering from retinal diseases. Our most advanced therapeutic product candidate is Zimura® (avacincaptad pegol), a complement C5 inhibitor. We recently announced positive initial, top-line data from a randomized, controlled clinical trial of Zimura in geographic atrophy, or GA, secondary to dry age-related macular degeneration, or AMD, which we believe may qualify as a pivotal clinical trial for regulatory purposes, and are commencing preparations for a second pivotal clinical trial of Zimura in this indication. We also believe that gene therapies using adeno-associated virus, or AAV, for gene delivery, hold tremendous promise for retinal diseases. We currently have two gene therapy product candidates in preclinical development and several collaborative gene therapy sponsored research programs ongoing. We plan to initiate clinical development of IC-100, our lead gene therapy product candidate, during the second half of 2020, subject to successful completion of preclinical development and regulatory review.

We are committed to the advancement of our therapeutic programs in parallel with our gene therapies. We recently announced initial, top-line data from our international, randomized, double masked, sham controlled multi-center clinical trial, which we refer to as our OPH2003 trial, assessing the safety and efficacy of Zimura for the treatment of GA. GA is the advanced stage of dry AMD and is characterized by retinal cell death and degeneration of tissue in the central portion of the retina, or the macula, which may result in loss of vision. The top-line data confirmed that Zimura met the prespecified primary endpoint in the trial in reducing the rate of GA growth in patients with dry AMD. The reduction in the mean rate of GA growth over 12 months was 0.110mm (p-value = 0.0072) for the Zimura 2 mg group as compared to the corresponding sham control group and 0.124mm (p-value = 0.0051) for the Zimura 4 mg group as compared to the corresponding sham control group, corresponding to an approximate 27% relative reduction in the mean rate of GA growth over 12 months when compared with sham. These data for both dose groups were statistically significant and we believe demonstrate a clinically relevant reduction in rate of GA growth. Based on our review of the safety data to date, Zimura was generally well tolerated over 12 months of administration in this clinical trial. Over this 12-month time period, there were no reported Zimura-related adverse events, no cases of Zimura-related intraocular inflammation, no ocular serious adverse events, no cases of Zimura related increase in intraocular pressure, no cases of endophthalmitis, and no discontinuations attributed by investigators to Zimura in the trial. We believe that the safety and efficacy results from the OPH2003 trial could potentially satisfy the FDA's requirements as one of the two pivotal clinical trials typically required for marketing approval. Based on the data we have received from the OPH2003 trial to date, we have commenced site selection and planning activities for a second pivotal clinical trial for Zimura in GA with the goal of initiating enrollment in this Phase 3 clinical trial during the first quarter of 2020. We plan to continue to explore all options for the future development and potential commercialization of Zimura, including potential collaboration and out-licensing opportunities, while we commence Phase 3 activities.

Our team has significant experience in the efficient execution of large-scale clinical trials for retinal diseases. We have deep relationships with global retina thought leaders, including those at a number of leading academic research institutions with which we have developed collaborative relationships, and an extensive network of ophthalmic clinical trial sites. We will seek to leverage these existing relationships as we prepare for our pivotal Phase 3 clinical trial for Zimura. We believe that the combination of these factors provides us a competitive advantage in retinal drug development.

Our therapeutics portfolio consists of two ongoing clinical trials evaluating Zimura and our preclinical development program of High temperature requirement A serine peptidase 1 protein, or HtrA1, inhibitors. In addition to the OPH2003 clinical trial of Zimura in GA, which remains ongoing, we have an ongoing randomized, double masked, sham controlled

clinical trial evaluating Zimura for the treatment of autosomal recessive Stargardt disease, or STGD1, which we refer to as our OPH2005 trial. We are developing our HtrA1 inhibitor program for GA and potentially other age-related retinal diseases. We previously evaluated Zimura in combination with Lucentis® (ranibizumab), an anti-vascular endothelial growth factor, or anti-VEGF, agent for the treatment of wet AMD, for which we completed a Phase 2a safety trial, which we refer to as the OPH2007 trial, during the fourth quarter of 2018.

Our gene therapy portfolio consists of several ongoing research and preclinical development programs that use AAV for gene delivery. These AAV gene therapy programs are targeting the following orphan IRDs:

- rhodopsin-mediated autosomal dominant retinitis pigmentosa, or RHO-adRP, which is characterized by progressive and severe bilateral loss of vision leading to blindness;
- IRDs associated with mutations in the BEST1 gene, including Best vitelliform macular dystrophy, or Best disease, which is generally characterized by bilateral egg yolk-like lesions in the macula, which, over time, progress to atrophy and loss of vision;
- Leber congenital amaurosis type 10, or LCA10, which is characterized by severe bilateral loss of vision at or soon after birth;
- autosomal recessive Stargardt disease, or STGD1, which is characterized by progressive damage to the macula and retina of young adults, leading to loss of vision; and
- IRDs associated with mutations in the USH2A gene, which include Usher syndrome type 2A, or Usher 2A, and USH2A-associated nonsyndromatic autosomal recessive retinitis pigmentosa.

Therapeutic Development Programs

Zimura Clinical Programs

Zimura, our complement C5 inhibitor, is a chemically-synthesized, pegylated RNA aptamer. We recently announced initial, top-line data from our OPH2003 clinical trial of Zimura for GA, and the trial remains ongoing. We also are conducting our OPH2005 clinical trial of Zimura for STGD1.

OPH2003 Clinical Trial: Assessing safety and efficacy of Zimura in GA secondary to dry AMD

At the end of October 2019, we announced initial, top-line data from OPH2003, an international, randomized, double masked, sham controlled, multi-center clinical trial evaluating the safety and efficacy of various doses of Zimura in patients with GA secondary to dry AMD. The primary efficacy analysis was performed at the 12-month time point, and the data we announced in October 2019 was for the first 12 months of the trial. Pursuant to the clinical trial protocol, patients will continue to be treated and followed through month 18 in order to collect additional data regarding Zimura in GA. We expect to remain masked regarding the treatment group to which each individual patient was randomized until the patient reaches month 18.

Trial Design and Enrollment

A total of 286 patients were enrolled across two parts of the trial.

Part 1. In Part 1 of the trial, 77 patients were randomized into one of three treatment groups in a 1:1:1 ratio as follows:

Cohort	**Zimura 1mg**	**Zimura 2mg**	**Sham**
Patients	26	25	26

In Part 1 of the trial, Zimura was administered by monthly intravitreal injections, while patients in the sham control group received monthly sham injections. In 2017, we modified the trial design to change the total number of patients to be enrolled, to change the primary endpoint from a vision endpoint to an anatomic endpoint, to shorten the time point for the primary efficacy analysis to month 12 and to include a Zimura 4mg dose group. The patients who were enrolled in Part 1 remained in the trial following these modifications.

Part 2. In Part 2 of the trial, we enrolled 209 additional patients, who were randomized into one of three treatment groups in a 1:2:2 ratio as follows:

Cohort	Zimura 2mg	Zimura 4mg	Sham
Patients	42	83	84

In Part 2 of the trial, patients in the Zimura 2mg group received one intravitreal injection of Zimura 2mg and one sham injection at each monthly visit; patients in the Zimura 4mg group received two intravitreal injections of Zimura 2mg at each monthly visit; and patients in the sham control group received two sham injections at each monthly visit. In its current formulation, doses of Zimura above 2mg would require more than one intravitreal injection.

The primary efficacy endpoint was the mean rate of growth of GA over 12 months, while secondary efficacy endpoints evaluated mean changes in patients' visual acuity in different lighting conditions over the same period.

Key Inclusion and Exclusion Criteria

In order to determine eligibility to participate in the trial, the location and size of each patient's GA was assessed using fundus autofluorescence, or FAF, images, which is a standard imaging modality used by retina specialists. An independent masked reading center assessed FAF images throughout the trial, including at baseline to determine eligibility.

The fovea is the central portion of the macula where visual acuity is the highest. We sought to enroll patients whose GA was located, in whole or in part, within 1500 microns of the foveal center but that did not enter the foveal center. A disc area is the size of the area of the retina where a standard sized optic nerve emerges, which is generally accepted to be $2.5mm^2$. We enrolled patients with a total GA area of between 1 and 7 disc areas (or $2.5mm^2$ to $17.5mm^2$) inclusive. If the GA was multifocal, meaning it was not continuous and had multiple locations, at least one focal lesion needed to measure at least 0.5 disc areas (or $1.25mm^2$). Each patient's best corrected visual acuity, or BCVA, was also assessed using the Snellen equivalent scale, which equates the detail a patient can see at a distance of 20 feet with the detail an individual with 20/20 vision can see at a greater distance. For example, a patient with 20/50 vision sees at 20 feet what a person with 20/20 vision would see at 50 feet. To be eligible to participate in the trial, patients' BCVA in the study eye was initially required to be between 20/25 and 20/100 inclusive during Part 1 of the trial. As part of the modifications we made for Part 2 of the trial, we expanded the inclusion criteria to include patients whose BCVA in the study eye was between 20/25 and 20/320 inclusive. BCVA on the Snellen equivalent scale can be equated to a number of letters of vision on the Early Treatment of Diabetic Retinopathy Study, or ETDRS, chart. BCVAs of 20/25, 20/100 and 20/320 on the Snellen equivalent scale are equivalent to 75 ETDRS letters, 50 ETDRS letters and 25 ETDRS letters, respectively.

Patients were stratified across treatment groups by baseline BCVA, baseline GA area and the baseline pattern of autofluorescence at the margins of the GA lesion, referred to as the junctional zone. Stratification for baseline characteristics is a method for allocating patients to treatment groups to ensure that there are approximately the same ratio of patients with a given baseline characteristic in each treatment group as the overall randomization ratio. For vision, patients were stratified based on whether their vision was above or below 50 ETDRS letters. For GA area, patients were stratified based on whether their GA area was above or below 4 disc areas. For autofluorescence pattern, patients were stratified based on several well-known patterns that have been described in the scientific literature.

Dry AMD progresses to the wet form of AMD in approximately 10% to 15% of AMD patients. Wet AMD occurs when new and abnormal blood vessels proliferate under or within the retina. These abnormal new blood vessels originate beneath the retina, in a layer called the choroid, and invade into the overlying retinal layers, and are referred to as choroidal neovascularization, or CNV. When we initiated the OPH2003 study, we did not believe that reliable measurement of GA by FAF for patients with CNV in the study eye could be performed. Therefore in the clinical trial protocol for the OPH2003 trial, we indicated that patients in any arm of the trial who developed CNV in the study eye would be removed from the trial and any future study treatments and assessments. We also excluded patients who had any evidence of CNV in either eye at their initial assessment. Patients who had a prior history of intravitreal treatment for any indication in either eye were excluded, as well as patients with any ocular condition in the study eye that could affect central vision or otherwise confound assessments.

Baseline Characteristics

We collected baseline characteristics for all patients participating in the trial. GA area was measured based on the area of GA in square millimeters (mm^2). Reported scientific literature indicate that the rate of GA growth may be dependent on the baseline lesion size, with larger GA lesions generally growing faster than smaller lesions, subject to an overall plateau effect as the GA grows to consume almost the entire macula. For this reason, patients were stratified in this trial based on their baseline

lesion size. To further mitigate for the impact of baseline lesion size on the growth of GA, a square root transformation was performed. It is reported in the scientific literature and accepted in the field that using the square root of the lesion size for calculating the mean change in size over time mitigates for the impact of the baseline lesion size. We used the square root transformation of GA area, measured in millimeters (mm) to perform the assessment of the primary efficacy endpoint in the OPH2003 trial.

In addition to measuring the area of GA, we followed patients for changes in their vision (BCVA), as measured both at a standard light level, or luminance, and lower light level, or low luminance (LL BCVA), measured in each case by ETDRS letters. Although GA can be associated with profound and irreversible vision loss, the vision loss that patients experience is not necessarily linearly correlated to the progression of GA. The specific location of the GA within patients' retinas can affect patients' vision differently. In general, patients whose GA expands into the fovea experience vision loss that is disproportionate to the vision loss experienced by patients whose GA does not expand into the fovea. Further, patients with GA may demonstrate good visual acuity but poor functional vision if their GA results in dark spots, referred to as scotomas, in their central visual field. Patients with scotomas may be able to read a vision chart letter-by-letter, especially if their GA has not entered the fovea, but they may have trouble reading a paragraph of text or driving, as these activities of daily living draw upon a field of vision that is broader than a single point of focus. For this reason, and based on our prior interactions with the FDA, we believe the efficacy assessment that is most likely to demonstrate clinical relevance for an investigational product across a heterogeneous GA patient population is reduced rate of growth in GA. If an investigational product can slow the growth of GA, it has the potential to preserve, or slow the loss of, functional vision for patients whose GA is expanding into critical areas of their central visual field, which would be clinically meaningful. Testing for visual acuity also serves as an important safety assessment to assure that the decrease in visual acuity in the Zimura treatment groups was not different from the sham control groups.

In addition to baseline GA area, it has been reported in the scientific literature that GA that is non-subfoveal, or that has not impacted the foveal center, is positively correlated with a higher rate of GA area progression and growth. We believe that once a GA lesion expands into the fovea, the rate of growth may be slowed. In addition, once GA expands to encompass the central fovea, additional progression can be limited in the central region of the retina, with any continued expansion occurring predominantly in the outer part of the retina.

For patients within each treatment group, where a numerical measurement was collected, we calculated the mean and standard deviation, or SD, for each measurement. SD is a statistical measure of the variability of a particular measurement within a patient population. Generally, two-thirds of all patients fall within approximately one SD, plus or minus, of the mean for any particular measurement.

The baseline characteristics of the patients who participated in the OPH2003 trial are presented below for each treatment group in each Part of the trial. Based on these data, we believe that the baseline characteristics were generally balanced across the treatment groups.

	Part 1			**Part 2**		
Cohort	**Zimura 1mg** (N = 26)	**Zimura 2mg** (N = 25)	**Sham** (N = 26)	**Zimura 2mg** (N = 42)	**Zimura 4mg** (N = 83)	**Sham 4mg** (N = 84)
Mean age, years (SD)	73.8 (8.0)	77.7 (9.6)	78.1 (8.4)	79.4 (10.7)	79.2 (8.3)	78.2 (9.0)
Female gender, number (%)	15 (57.7%)	18 (72.0%)	18 (69.2%)	27 (64.3%)	58 (69.9%)	61 (72.6%)
Active smokers, number (%)	6 (23.1%)	10 (40.0%)	7 (26.9%)	15 (35.7%)	26 (31.3%)	29 (34.5%)
Caucasian race, number (%)	25 (96.2%)	25 (100%)	25 (96.2%)	42 (100%)	82 (98.8%)	82 (97.6%)
Iris color:						
Light	13 (50.0%)	16 (64.0%)	17 (65.4%)	29 (69.0%)	54 (65.1%)	57 (67.9%)
Medium	7 (26.9%)	6 (24.0%)	7 (26.9%)	9 (21.4%)	22 (26.5%)	21 (25.0%)
Dark	6 (23.1%)	3 (12.0%)	2 (7.7%)	4 (9.5%)	7 (8.4%)	6 (7.1%)
Mean intraocular pressure, mmHg (SD)	15.0 (1.9)	14.6 (2.6)	14.5 (2.8)	14.1 (2.4)	15.2 (2.5)	14.9 (2.5)
Non-subfoveal GA, number (%)	23 (88.5%)	20 (80.0%)	22 (84.6%)	42 (100%)	81 (97.6%)	82 (97.6%)
Mean GA area, mm^2 (SD)	7.37 (4.32)	6.60 (3.35)	7.33 (3.73)	7.77 (4.01)	7.90 (4.18)	7.45 (3.89)
Mean Sq. Root of GA area, mm (SD)	2.591 (0.827)	2.471 (0.717)	2.623 (0.687)	2.705 (0.684)	2.715 (0.732)	2.636 (0.709)
Bilateral GA, number (%)	26 (100%)	25 (100%)	25 (96.2%)	42 (100%)	83 (100%)	83 (98.8%)
Mean BCVA, ETDRS letters (SD)	70.5 (8.0)	71.6 (7.5)	71.3 (7.5)	69.4 (11.3)	69.5 (9.8)	68.3 (11.0)
Mean LL BCVA, ETDRS letters (SD)	38.1 (22.7)	43.0 (19.7)	36.7 (21.2)	33.1 (21.3)	36.8 (20.9)	33.9 (18.8)
Patients with Hyperautofluorscence (%)	25 (96.2%)	25 (100%)	26 (100%)	41 (97.6%)	82 (98.8%)	83 (98.8%)
Height, cm (SD)	168.7 (12.0)	165.9 (8.6)	164.9 (12.1)	164.9 (11.0)	163.7 (10.6)	163.7 (9.3)
Weight, kg (SD)	81.9 (17.8)	75.6 (14.9)	74.7 (15.6)	80.8 (22.3)	76.2 (18.2)	78.4 (17.8)

12-Month Safety Data

Based on our review of the safety data to date, Zimura was generally well tolerated after 12 months of administration. Over this 12-month time period, there were no reported ocular serious adverse events, no Zimura-related adverse events, no cases of Zimura-related intraocular inflammation, no cases of Zimura-related increased intraocular pressure, no cases of endophthalmitis, and no discontinuations attributed by investigators to Zimura in the trial.

The number of patients with one or more serious, systemic, treatment emergent adverse events, organized by MedDRA system organ class, a standard method of reporting adverse events, are set forth in the table below:

Patients with One or More Serious Treatment Emergent Adverse Events (TEAEs) in Any Organ Class

	Part 1			**Part 2**		
	Zimura 1mg (N = 26)	**Zimura 2mg** (N = 25)	**Sham** (N = 26)	**Zimura 2mg** (N = 42)	**Zimura 4mg** (N = 83)	**Sham 4mg** (N = 84)
Cardiac disorders	1 (3.8%)	0	0	0	2 (2.4%)	3 (3.6%)
Gastrointestinal disorders	1 (3.8%)	1 (4.0%)	1 (3.8%)	0	2 (2.4%)	6 (7.1%)
General disorders and administration site conditions	0	0	0	1 (2.4%)	0	0
Hepatobiliary disorders	0	1 (4.0%)	1 (3.8%)	0	1 (1.2%)	0
Infections and infestations	0	1 (4.0%)	0	1 (2.4%)	6 (7.2%)	2 (2.4%)
Injury, poisoning and procedural complications	0	1 (4.0%)	0	1 (2.4%)	3 (3.6%)	2 (2.4%)
Metabolism and nutrition disorders	0	0	1 (3.8%)	0	0	0
Musculoskeletal and connective tissue disorders	1 (3.8%)	0	0	0	0	2 (2.4%)
Benign, malignant and unspecified neoplasms (including cysts and polyps)	0	0	0	0	1 (1.2%)	2 (2.4%)
Nervous system disorders	1 (3.8%)	1 (4.0%)	1 (3.8%)	1 (2.4%)	3 (3.6%)	1 (1.2%)
Psychiatric disorders	0	0	1 (3.8%)	0	0	1 (1.2%)
Respiratory, thoracic and mediastinal disorders	0	1 (4.0%)	0	0	2 (2.4%)	3 (3.6%)

The number of patients with one or more systemic TEAEs, including serious systemic TEAEs, identified by the investigator as related to the study drug (Zimura or sham) are set forth in the table below:

Reported Systemic Treatment Emergent Adverse Events (TEAEs) Related to Zimura or Sham

	Part 1			**Part 2**		
	Zimura 1mg (N = 26)	**Zimura 2mg** (N = 25)	**Sham** (N = 26)	**Zimura 2mg** (N = 42)	**Zimura 4mg** (N = 83)	**Sham 4mg** (N = 84)
Subjects with at least one TEAE	0	0	0	0	0	0

The number of patients with one or more ocular TEAEs in the study eye are set forth in the table below:

Reported Ocular TEAEs in Study Eyes

	Part 1			**Part 2**		
	Zimura 1mg (N = 26)	**Zimura 2mg** (N = 25)	**Sham** (N = 26)	**Zimura 2mg** (N = 42)	**Zimura 4mg** (N = 83)	**Sham 4mg** (N = 84)
Eye disorders	12 (46.2%)	8 (32.0%)	4 (15.4%)	24 (57.1%)	50 (60.2%)	33 (39.3%)
Eye disorders related to injection procedure	3 (11.5%)	4 (16.0%)	2 (7.7%)	14 (33.3%)	36 (43.4%)	23 (27.4%)

All of the above TEAEs that were not related to the injection procedure were also not related to the study drug. The number of patients with one or more ocular TEAEs in the study eye, identified by the investigator as related to the study drug (Zimura or sham) is set forth in the table below:

Reported Ocular TEAEs in the Study Eye Related to Zimura or Sham

	Part 1			Part 2		
	Zimura 1mg (N = 26)	**Zimura 2mg** (N = 25)	**Sham** (N = 26)	**Zimura 2mg** (N = 42)	**Zimura 4mg** (N = 83)	**Sham 4mg** (N = 84)
Subjects with at least one TEAE	0	0	0	0	0	0

Incidence of CNV. During the first 12 months of this trial, the incidence of CNV in the untreated fellow eyes was 10 patients (3.5%) and in the study eyes was 3 patients (2.7%) in the sham group, 1 patient (4.0%) in the Zimura 1mg group, 6 patients (9.0%) in the Zimura 2mg group, and 8 patients (9.6%) in the Zimura 4mg group.

Statistical Analysis for Efficacy Measures

OPH2003 was designed as a Phase 2b screening trial based on the criteria described by Drs. Thomas Fleming and Barbara Richardson in their publication regarding clinical trial design in the context of microbicides for the prevention of HIV in the Journal of Infectious Disease in 2004. A screening trial uses the same primary efficacy endpoint as an anticipated Phase 3 clinical trial that would be used to support potential regulatory approval. However, screening trials generally have a considerably smaller sample size than the anticipated Phase 3 clinical trial. Because it is particularly important to avoid false negative outcomes in a screening trial, screening trials may have higher false positive error rates than would typically be allowed in a Phase 3 trial.

A Phase 2b screening trial has three possible outcomes:

- If the estimated effect size indicates low levels of benefit, the experimental intervention would be judged as not plausibly more efficacious than the sham control, and should be discarded in its current dosage in the indication evaluated; or

- If the estimated effect size is moderate but clinically relevant, with a relatively low likelihood of being achieved (for example, a probability of less than 10%), if there truly were no effect, the experimental intervention would be judged as plausibly more efficacious than the sham control and should be evaluated definitively in subsequent Phase 3 clinical trials.

- If the estimated effect size is clinically relevant and reaches the traditional threshold for statistical significance, as was the case in the OPH2003 trial for both the Zimura 2mg and Zimura 4mg dose groups as compared to the corresponding sham control groups, the trial could potentially serve as one of the two pivotal trials typically required for regulatory approval.

A properly designed Phase 2b screening trial has a considerable likelihood of ruling out ineffective or harmful interventions, while providing encouraging (or even statistically significant) evidence of benefit that likely would require confirmation by one additional, independent Phase 3 trial.

For the primary and secondary efficacy analysis, we evaluated the ITT, or intent-to-treat, population, which includes all patients who were randomized in the trial and who received at least one dose of study drug in the relevant treatment group.

The statistical evidence from the OPH2003 trial regarding the comparison of Zimura 2 mg to sham control is provided by data from both Part 1, with a 1:1 randomization ratio of patients to Zimura 2mg (25 patients) and to sham (26 patients), as well as data from Part 2, with a 1:2 randomization ratio of patients to Zimura 2mg (42 patients) and to sham (84 patients), for a total of 67 patients receiving Zimura 2mg and 110 patients receiving sham. While we believe it is fully appropriate to use the aggregate data from Parts 1 and 2 in the analysis of the relative effects of Zimura 2mg as compared to sham, it would not be appropriate to simply pool the data from patients in both Parts 1 and 2, in particular, because the randomization fraction differs across these two parts of the trial. However, based on the randomization procedures used in each part of the trial, for purposes of statistical comparisons, within Part 1 of the trial, the 25 patients receiving Zimura 2mg should be comparable to the 26 patients receiving sham. Similarly, for purposes of statistical comparisons, within Part 2 of the trial, the 42 patients receiving Zimura 2mg should be comparable to the 84 patients receiving sham. The efficacy of Zimura 2mg was therefore evaluated through an analysis which included a regression factor by trial part. The statistical analysis for the Zimura 4mg group as compared to sham compares data for patients from Part 2 of the trial only. Data from patients receiving Zimura 1mg in Part 1 of the trial was not part of the prespecified statistical analysis for the efficacy endpoints.

The prespecified statistical analysis plan for the primary and secondary endpoints of this trial used a model of repeated measures, or MRM, to compare data for the Zimura 2mg and Zimura 4mg groups to the corresponding sham groups. MRM analysis is a commonly used method to interpret and analyze a longitudinal data set that may be missing data points. During the course of a clinical trial, patients may withdraw from the clinical trial because their condition is asymptomatic, because patients believe that continued participation in the trial is not justified based on the time commitment or treatment burden, such as receiving monthly intravitreal injections, at the recommendation of the investigator or because the protocol requires it. Additionally, patients may not come to a scheduled visit at which key assessments are scheduled to be taken or patient data may not be evaluable because of poor image quality or data recording errors. Early withdrawal, missed visits and unevaluable data all result in data missing from the final data set for a clinical trial. Although the protocol called for collection of FAF images of GA at baseline, at month 6 and at month 12, for patients who withdrew from the trial before month 12, the study protocol required the collection of an FAF image to provide a measurement of GA at the time of withdrawal, which was included in the primary analysis so long as it was taken within the month prior to month 6 or month 12 time point. The MRM analysis would need measurements from at least two different time points for modeling purposes and therefore patients with at least two GA measurements were included in the analysis.

The following table sets forth for the data in the primary statistical analysis the number of patients for whom GA measurements were missing for purposes of performing this analysis. Patients whose GA measurements were missing at baseline, or at month 6 and month 12, could not be included in the primary analysis. All other patients were included in the primary analysis.

Cohort	**Zimura 2mg** (N = 67)	**Sham 2mg** (N = 110)	**Zimura 4mg** (N = 83)	**Sham 4mg** (N = 84)
Missing GA measurement at BL, M6 and M12	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Missing GA measurement at M6 and M12 only	8 (11.9%)	11 (10.0%)	17 (20.5%)	5 (6.0%)
Missing GA measurement at BL only	0 (0%)	0 (0%)	1 (1.2%)	0 (0%)
Total patients excluded from MRM analysis	8 (11.9%)	11 (10%)	18 (21.7%)	5 (6.0%)
Missing GA measurement at M6 only	1 (1.5%)	7 (6.4%)	3 (3.6%)	6 (7.1%)
Missing GA measurement at M12 only	10 (14.9%)	9 (8.1%)	11 (13.3%)	7 (8.3%)
No missing GA measurements[(a)]	48 (71.6%)	83 (75.5%)	51 (61.5%)	66 (78.6%)
Total patients included in MRM analysis	59 (88.0%)	99 (90.0%)	65 (78.3%)	79 (94.1%)

BL = Baseline; M6 = Month 6; M12 = Month 12

(a) = complete observations

In total, 53 (18.5%) of patients withdrew from the trial during the first 12 months. Of the patients who withdrew during the first 12 months, 2 patients were from the Zimura 1mg group (7.7% withdrawals), 12 patients were from the combined Zimura 2mg group (17.9% withdrawals), 25 patients were from the Zimura 4mg group (30.1% withdrawals) and 14 patients were from the combined sham group (12.7% withdrawals). GA measurements for patients who withdrew from the study prior to the month 12 time point may have been included in the MRM analysis, as detailed in the table above.

Sensitivity analyses. We performed several sensitivity analyses to assess the impact of missing data on the robustness of the OPH2003 trial results. The analyses we performed were based on approaches that the FDA generally recommends sponsors of investigational products use to evaluate their clinical data. Based on these analyses, and accounting for the data missing from our data set because of patient withdrawals or for other reasons, the statistical analysis for the 12 month data from the OPH2003 clinical trial appear to be robust. Descriptions of these sensitivity analyses and their outcomes are summarized below. For a description of the thresholds we used to determine statistical significance on the primary efficacy endpoint, see the paragraph below the tables below under "Primary Efficacy Endpoint Data."

- A "shift imputation" approach, in which missing data are imputed, or replaced, by values calculated from similar patients with observed values, plus a defined shift. The analysis is repeated assuming a progressively larger shift with each iteration. The analysis becomes increasingly conservative as the shift increases (because missing values are replaced by worse values than would have been observed, had the values not been missing). The shift is increased until a tipping point is reached and statistical significance is lost. If significance is lost for smaller shift values, the results of the analyses are sensitive to missing data, whereas if significance is lost for larger shift values, the results of the analyses are robust to missing data.

  A shift of at least 0.05mm in terms of square root of GA was required to lose statistical significance for both the Zimura 2mg and Zimura 4mg groups. The difference between the Zimura treatment groups and the corresponding

sham groups, in terms of mean change of square root of GA, was 0.11mm for the Zimura 2mg group and 0.12mm for the Zimura 4mg group, so a shift of 0.05mm represents more than 40% of the observed treatment effect, which is large.

- Arbitrary imputation approaches, in which missing data are replaced by:
  - the mean value of same treatment group, which seems a reasonable imputation approach since it replaces missing values by the mean of all observed values in the same treatment group;
  - the mean value of comparator treatment group, which is a very conservative approach. If there is a treatment effect, missing values in the sham control group are replaced by better values, on average, from the Zimura treatment group, while missing values in the Zimura treatment group are replaced by worse values, on average, from the sham control group;
  - the mean value of both treatment groups, which is a conservative approach because it assumes no treatment effect for missing values; and
  - the mean value of the sham control group, which is also a conservative approach because it draws only upon data from the sham control group, which by definition did not have any treatment benefit.

  Statistical significance for the reduction in mean rate of GA growth for the Zimura 2mg and Zimura 4mg groups as compared to the corresponding sham groups was retained for all arbitrary imputation approaches.
- A “pattern mixture model imputation” approach, which is a technically complex model and is especially useful when data are suspected to be missing “not at random”.

  Statistical significance for the reduction in mean rate of GA growth for the Zimura 2mg and Zimura 4mg groups as compared to the corresponding sham groups was retained for the pattern mixture model imputation approach, which suggests again that the results of the analyses are robust to missing data, even if these data had been missing not at random.

Based on our sensitivity analyses, and accounting for the data missing from our data set because of patient withdrawals or for other reasons, we believe the statistical analysis for the 12 month data from the OPH2003 clinical trial is robust.

Primary Efficacy Endpoint Data

The prespecified primary efficacy endpoint was an anatomic endpoint, the mean change in rate of GA growth over 12 months, as measured by FAF based on readings at three time points: baseline, month 6 and month 12, calculated using the square root transformation of the GA area. The readings were performed by an independent masked reading center. The primary efficacy endpoint data are summarized in the following table:

Mean Rate of Change in Geographic Atrophy (GA) Area from Baseline to Month 12

(MRM Analysis) (Square Root Transformation)

Cohort	**Zimura 2mg** (N = 67)	**Sham 2mg** (N = 110)	**Difference**	**P-value**	**% Difference**
Mean Change in GA[(a)] (mm)	0.292[(b)]	0.402[(b)]	0.110	0.0072[(c)]	27.38%

Cohort	**Zimura 4mg** (N = 83)	**Sham 4mg** (N = 84)	**Difference**	**P-value**	**% Difference**
Mean Change in GA[(a)] (mm)	0.321	0.444	0.124	0.0051[(c)]	27.81%

(a) = based on the least squared means from the MRM model.
(b) = these least squared means are estimates from the MRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data.
(c) = reflects statistically significant p-value; Hochberg procedure was used for significance testing.

The analysis of the mean change in GA for Zimura 2mg *vs.* Sham 2mg was adjusted for the fact that this dose of Zimura was tested in the two parts of the trial, which had different randomization ratios. The least squared mean changes in GA in Part 1 and Part 2 are shown separately in the following table:

Mean Rate of Change in Geographic Atrophy (GA) Area from Baseline to Month 12
(MRM Analysis) (Square Root Transformation)

Cohort		Zimura 2mg (N = 25)	Sham 2mg (N = 26)	Difference
Part 1	Mean Change in GA[(a)] (mm)	0.329	0.422	0.093

(a) = based on the least squared means from the MRM model

Cohort		Zimura 2mg (N = 42)	Sham 2mg (N = 84)	Difference
Part 2	Mean Change in GA[(a)] (mm)	0.308	0.422	0.114

(a) = based on the least squared means from the MRM model

When the data from the Zimura 2mg comparisons from each Part of the trial are combined in the MRM model, the mean difference in GA growth over 12 months between the Zimura 2mg and sham control groups is 0.110 mm, as indicated in the combined analysis in the tables above.

Statistical significance is established by performing statistical analysis on a data set to assess the degree to which an observed outcome is likely to be associated with variability in the studied patient population or chance as compared to the impact of the investigational product being studied. A higher degree of statistical significance is associated with a lower p-value. Typically, a two-sided p-value of 0.05 or less represents statistical significance when performing only a single prespecified primary analysis for a single primary endpoint. However, when multiple doses of a drug are tested a more stringent statistical method that accounts for multiple comparisons must be applied. For this purpose, we used the Hochberg multiple comparison procedure to assess the statistical significance of the results observed in the OPH2003 trial. Under the Hochberg procedure, it is necessary to use a stricter standard for statistical significance (a two-sided p-value of 0.025 or less) for any particular dose. For OPH2003, the results for the primary efficacy endpoint observed for both the Zimura 2mg and Zimura 4mg groups, as compared to the corresponding sham group, achieved p-values of 0.0072 and 0.0051, respectively, both of which are less than 0.025, indicating that both results were statistically significant.

Secondary Efficacy Endpoints Data

The prespecified secondary endpoints in this trial were the mean change in BCVA (ETDRS letters) from baseline to month 12 and the mean change in LL BCVA (ETDRS letters) from baseline to month 12. As we believe that BCVA may not be the optimal assessment to evaluate the impact of GA on patients' functional vision, we included vision in the prespecified analysis as a secondary, and not as a primary, endpoint. Testing for visual acuity also serves as an important safety assessment to assure that the decrease in visual acuity in the Zimura treatment groups was not different from the sham control groups.

The OPH2003 trial was not designed to reliably assess differences in mean changes in BCVA or LL BCVA with statistical significance. Data for the secondary endpoints are summarized in the following tables:

Mean Change in Best Corrected Visual Acuity (BCVA) from Baseline to Month 12
(MRM Analysis) (ETDRS letters)

Cohort	Zimura 2mg (N = 67)	Sham 2mg (N = 110)	Difference
Mean Change in BCVA[(a)]	-7.90[(b)]	-9.29[(b)]	1.39

Cohort	Zimura 4mg (N = 83)	Sham 4mg (N = 84)	Difference
Mean Change in BCVA[(a)]	-3.79	-3.51	-0.28

(a) = based on the least squared means from the MRM model
(b) = these least squared means are estimates from the MRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data.

Mean Change in Low Luminance Best Corrected Visual Acuity (LL BCVA) from Baseline to Month 12
(MRM Analysis) (ETDRS letters)

Cohort	Zimura 2mg (N = 67)	Sham 2mg (N = 110)	Difference
Mean Change in LL BCVA[a]	-1.03[b]	-1.41[b]	0.38

Cohort	Zimura 4mg (N = 83)	Sham 4mg (N = 84)	Difference
Mean Change in LL BCVA[a]	1.53	2.97	-1.44

(a) = based on the least squared means from the MRM model
(b) = these least squared means are estimates from the MRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data.

Zimura 1mg 12-Month Efficacy Data.

Efficacy data from patients receiving Zimura 1mg was not part of the prespecified statistical analysis. The total number of patients randomized to the Zimura 1mg group (26 patients) is relatively small, and the trial was not powered to reliably assess differences in outcomes for these patients as compared to patients in the sham control group in Part 1 (26 patients). However, we performed descriptive analyses on the 12 month data for patients in the Zimura 1mg as compared to the patients in the sham control group in Part 1 of the trial to aid our assessment of whether a dose response relationship was present across treatment groups included in the clinical trial.

GA area data for the Zimura 1mg group and the sham group from Part 1 of the trial are summarized in the following tables:

Summary of Geographic Atrophy (GA) Area (mm) and Mean Percentage Change from Baseline to Month 12
(Square Root Transformation)

Cohort	Zimura 1mg (N = 26)	Sham Part 1 (N = 26)
Mean Sq. Root of GA at BL, mm (SD)	2.591 (0.827)	2.623 (0.687)
Mean Sq. Root of GA at M12, mm (SD)	3.055 (0.604)	3.021 (0.722)
Difference	0.464	0.398
Mean % Change[a] (SD)	14.48% (8.2%)	16.49% (7.2%)

BL = Baseline; M12 = Month 12
(a) Mean % Change in GA area is an average of the percentage change in GA area observed for each patient.

Although the sample size for the Zimura 1mg group is small, we believe the apparent reduction in mean percentage change in GA area from baseline to month 12 in the Zimura 1mg group as compared to the sham control group in Part 1, when combined with the statistically significant results observed for the primary efficacy endpoint for the Zimura 2mg and Zimura 4mg groups as compared to their corresponding sham control groups, is suggestive of a potential dose response relationship across treatment groups.

Anticipated 18-Month Data

In accordance with the clinical trial protocol, we will continue to treat and follow patients over 18 months to collect additional data for Zimura in GA. Once all patients reach the 18 month time point, we expect that we will receive unmasked individual patient data for all evaluations performed throughout the trial, and, for each treatment group, mean change in the GA lesion area over 18 months and mean BCVA and mean LL BCVA at month 18. We are not planning to perform any prespecified statistical analyses with respect to the 18 month data as the trial was not designed to reliably assess differences between the Zimura treatment groups and corresponding sham control groups.

Requirements for Regulatory Approval of Zimura in GA

To obtain regulatory approval for Zimura for the treatment of geographic atrophy secondary to dry AMD, we expect that we will need to obtain favorable results from a total of two adequate and well-controlled pivotal clinical trials, demonstrating the safety and efficacy of Zimura in this indication. To establish efficacy, we believe it would be sufficient to demonstrate robust, statistically significant results showing a clinically relevant reduction in the rate of growth of GA over 12 months, based on measurements over three time points (baseline, month 6 and month 12). We selected this measure as the primary endpoint for the OPH2003 trial based on our prior interactions with the FDA, as well as our understanding of clinical trials for other investigational products in development for the treatment of GA. We designed the OPH2003 trial as a well-controlled screening trial such that, in the event that the prespecified primary efficacy endpoint results were statistically significant, the trial could potentially qualify as a pivotal clinical trial for registration purposes. Based on the results we have received, the statistical analysis that we have performed and preliminary, informal discussions we have had with the FDA, we believe that the safety and efficacy results from our OPH2003 international, randomized, double masked, sham controlled, multi-center clinical trial could potentially satisfy the FDA's requirements as one of the two pivotal clinical trials typically required for marketing approval. In the paragraphs that follow, we describe in detail the basis for our belief.

Requirements for Safety Data

Zimura has generally been well tolerated in our clinical trials to date. Over the 12-month time point for all patients in the OPH2003 trial, there were no reported ocular serious adverse events, no Zimura-related adverse events, no cases of Zimura-related intraocular inflammation, no cases of Zimura-related increased intraocular pressure, no cases of endophthalmitis, and no discontinuations attributed by investigators to Zimura in the trial. We believe the observed CNV incidence rate in the study eye for patients receiving Zimura as compared to sham and the untreated fellow eyes during the first 12 months of the trial is within an acceptable range when compared to published clinical trial data for another complement inhibitor currently in development for GA. The most frequently reported ocular adverse events in the OPH2003 trial were related to the injection procedure.

To demonstrate the safety of Zimura to a degree sufficient to support approval, we believe that the FDA and EMA would require data from a minimum of 300 patients having received the dose of Zimura for which we are seeking approval, or a higher Zimura dose, for a minimum of 12 months, with 24-month safety data available for some portion, but not all, of these 300 patients. Including patients randomized to the Zimura 4mg group in the OPH2005 trial of Zimura for STDG1, we expect that we will have 12-month safety data for approximately 145 patients who will have received monthly Zimura 2mg or Zimura 4mg once we receive initial top-line data from the OPH2005 clinical trial during the second half of 2020. Therefore, based on the safety profile of Zimura observed in these patients to date and the number of patients treated, we believe that the remaining minimum safety requirements could potentially be satisfied through a single additional, pivotal clinical trial providing for monthly administration of Zimura over 12 months, at which point the primary efficacy analysis would be performed, with treatment extending to 24 months for the overall safety analysis, with the potential for less frequent dosing regimen after month 12.

Requirements for Efficacy Data

As described above, we believe that reduction in the rate of GA growth over 12 months, based on measurements over three time points (baseline, month 6 and month 12) is an efficacy endpoint that the FDA and EMA would likely accept in considering Zimura for approval for the treatment of GA secondary to dry AMD. The measurements for this endpoint are performed by a masked independent reading center to minimize the potential for bias.

Statistical Significance. In our OPH2003 trial, the reduction in the mean rate of GA growth over 12 months was 0.110 mm (p-value = 0.0072) for the Zimura 2 mg group as compared to the corresponding sham control group and 0.124 mm (p-value = 0.0051) for the Zimura 4 mg group as compared to the corresponding sham control group, corresponding to an approximate 27% relative reduction in the mean rate of GA growth over 12 months when compared with sham. These data for both dose groups were statistically significant. See above under "Primary Efficacy Endpoint Data" for a discussion of the procedures we used to verify the statistical significance of these data.

Clinical Relevance. Clinical relevance refers to an assessment of how meaningful the observed outcome is or would be for patients. The FDA and other regulatory authorities consult with clinicians in the field of study to advise on the relevance of an observed outcome for patients. As there are no FDA or EMA approved therapies for the treatment of GA secondary to dry AMD, we do not yet know for certain what outcomes the FDA and other regulatory authorities will consider to be clinically relevant for this indication. However, since established literature and clinical experience indicates that patients functional vision is impacted by the growth of the GA over time, which ultimately leads to severe vision loss, we believe that reduction of GA growth would have a meaningful impact on the patients' well-being and quality of life and therefore is clinically relevant.

To secure approval to market an investigational product, a sponsor must demonstrate to the applicable regulatory authority that the potential benefits to be conferred to patients outweigh the potential risks associated with a treatment.

Robustness. In addition to statistical significance and clinical relevance, data from pivotal clinical trials must be robust. The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use defines robustness as a concept that refers to the sensitivity of the overall conclusions to various limitations of the data, assumptions, and analytic approaches to data analysis. OPH2003 is an international, randomized, double masked, sham controlled, multi-center clinical trial. The primary endpoint is an objective anatomic endpoint based on measurements performed by a masked independent reading center. The images are analyzed by two experienced image readers, with any discrepancy of greater than 10% arbitrated by the reading center director, who is a recognized expert in the field of GA.

In clinical trials, it is common for data for some number of subjects to be missing for assessments performed throughout the trial. The degree of data that is missing from a clinical data set can impact the robustness of the data. See above under "Statistical Analysis for Efficacy Measures" for information regarding the GA measurement data that was missing from the analysis of the primary efficacy endpoint in the OPH2003 trial, as well as a description of the sensitivity analyses we have performed. Based on our sensitivity analyses, and accounting for the data missing from our data set because of patient withdrawals or for other reasons, we believe the statistical analysis for the 12 month data from the OPH2003 trial is robust.

Although we seek to apply our enrollment criteria consistently, there may be instances where an investigator proposes a patient to participate in the trial and the reading center determines that, although a patient may not meet all criteria precisely, participation in the trial is warranted based on the overall GA pattern and size. For example, this can result in the enrollment of patients with baseline GA area slightly below 1 disc area, as was the case with one patient each in the Zimura 4mg group and the Part 2 sham control group (which is part of the comparison for both the Zimura 2mg and Zimura 4mg groups). These patients have been included in the ITT analysis for our primary efficacy endpoint. The FDA, EMA or other regulatory authorities may not agree with the inclusion of these patients in our statistical analysis, which could impact the robustness of our conclusions.

Currently, the trial is ongoing and patients continue to be treated and followed for an additional six months after the 12-month time point. We do not expect to receive the full data set with individual patient data unmasked as to treatment group until after the month 18 visit is completed for all patients. It is possible that unexpected or inconsistent findings could emerge based on additional data we receive for the period between months 12 and 18 or based on the full data set with unmasked, individual patient data. We may uncover individual patient data that causes us to re-evaluate and potentially change our initial conclusions based on the data we have received and our sensitivity analyses performed to date. Ultimately, for the OPH2003 trial to be accepted as a pivotal trial, the FDA, EMA and other regulatory authorities would need to agree that the overall data package from the OPH2003 trial and a subsequent pivotal clinical trial meet the applicable requirements and are sufficiently robust to demonstrate an acceptable safety profile, together with a clinically relevant efficacy outcome with statistical significance, and support an overall favorable benefit-to-risk determination.

Phase 3 Design and Activities

Based on the foregoing, assuming that Zimura's safety profile remains consistent with findings observed to date and subject to regulatory review of the robustness of the OPH2003 trial results, we believe that one additional international, randomized, double masked, sham controlled, pivotal Phase 3 clinical trial may be needed to demonstrate the safety and efficacy of Zimura in GA secondary to dry AMD in a manner sufficient to support an application for regulatory approval from the FDA and EMA in this indication. We expect that such a randomized, sham controlled, pivotal Phase 3 clinical trial would include a primary efficacy analysis at 12 months, with patients continuing to be treated and followed for a total of 24 months. Patients would likely receive monthly administrations of Zimura or monthly sham injections for the first 12 months of the trial, with the potential to modify the treatment regimen for less frequent administrations during the second 12 months. We will continue to analyze the OPH2003 data to determine the number of patients this Phase 3 clinical trial would likely need to include, as well as the relevant dose level or levels, to potentially demonstrate a clinically relevant outcome with statistical significance and to satisfy the safety requirements of the FDA and other regulatory authorities.

We expect that the design of the Phase 3 clinical trial, including the inclusion and exclusion criteria and primary outcome measure, would be similar to the design used for the OPH2003 trial, although we may potentially modify the protocol for patients who develop CNV in the study eye during the trial. As discussed above, when we initiated the OPH2003 study, we did not believe that reliable measurements of GA by FAF images for patients with CNV in the study eye could be performed. Therefore, in the clinical trial protocol for the OPH2003 trial, we indicated that patients in any arm of the trial who developed CNV in the study eye would be removed from the trial and any future study treatments and assessments. Based on additional third-party clinical data published since the OPH2003 trial commenced, we believe that GA for patients developing CNV in the study eye (and who receive standard of care anti-VEGF treatment for the CNV) could potentially be assessed reliably by FAF. Pending discussions with our independent reading center, we may modify the protocol for the Phase 3 trial, as compared to the protocol for OPH2003, to provide that patients who develop CNV in the study eye will remain in the trial and continue to receive the study drug, standard of care anti-VEGF treatment, and be followed to collect additional data to be included in our analysis. We also may evaluate additional secondary efficacy endpoints, in addition to, or in lieu of mean change in BCVA and mean change in LL BCVA.

Our belief and understanding of the remaining clinical requirements to demonstrate the safety and efficacy of Zimura for the treatment of GA secondary to dry AMD in a manner sufficient to support an application for regulatory approval from the FDA and EMA is based on our review of initial, top-line data from the OPH2003 trial as well as preliminary, informal discussions with the FDA. Our expectations regarding the minimum clinical requirements to demonstrate the safety and efficacy of Zimura for GA may change as we continue to review and analyze the OPH2003 12-month clinical data set, as 18-month clinical data from OPH2003 becomes available, and as new regulatory or third party information becomes available.

We have commenced site selection and planning activities for the Phase 3 clinical trial for Zimura in GA. We have drug supply available to begin such a trial and plan to begin enrolling patients in the trial during the first quarter of 2020.

OPH2005: Phase 2b Clinical Trial for Autosomal Recessive Stargardt Disease (STGD1)

OPH2005 is an ongoing, randomized, double masked, sham controlled, multi-center Phase 2b clinical trial evaluating the safety and efficacy of Zimura for the treatment of STGD1. Similar to OPH2003, OPH2005 was designed to be a Phase 2b screening trial, with the potential to demonstrate statistically significant results depending on the magnitude of the potential benefit observed. We completed enrollment for this clinical trial in February 2019 with a total of 95 patients enrolled. This trail remains on track and we expect that initial, top-line data from this clinical trial will be available during the second half of 2020.

HtrA1 Inhibitor Program

We are pursuing the preclinical development of certain HtrA1 inhibitors, to which we acquired rights through our October 2018 acquisition of Inception 4, Inc., or Inception 4, for the treatment of GA secondary to dry AMD. Our HtrA1 inhibitor program includes a number of lead small molecule compounds that show high affinity and specificity for HtrA1 when tested, as well as a number of backup compounds. We are pursuing process development and formulation development with the goal of identifying a viable manufacturing process and a formulation for intravitreal application in the eye. If we are successful in identifying a viable manufacturing process for and formulating a product candidate from this program, we plan to initiate IND-enabling activities for the selected product candidate. Based on current timelines and subject to successful completion of preclinical development and regulatory review, we plan to file an IND for a product candidate from this program during 2021.

Gene Therapy Research and Development Programs

IC-100: Product Candidate for RHO-adRP

We are pursuing the preclinical development of IC-100, our novel AAV gene therapy product candidate for the treatment of RHO-adRP. We acquired exclusive development and commercialization rights to IC-100 through a June 2018 license agreement with the University of Florida Research Foundation, or UFRF, and the University of Pennsylvania, or Penn. We and Penn are conducting additional preclinical studies of IC-100 and a natural history study of RHO-adRP patients. In parallel, we have engaged a gene therapy contract development and manufacturing organization, or CDMO, as the manufacturer for preclinical and Phase 1/2 clinical supply of IC-100. Process development is ongoing and we are planning for Phase 1/2 clinical manufacturing and other IND-enabling activities. Based on current timelines and subject to regulatory review, we expect to initiate a Phase 1/2 clinical trial for IC-100 during the second half of 2020.

IC-200: Product Candidate for BEST1-Related IRDs

We are pursuing the preclinical development of IC-200, our novel AAV gene therapy product candidate for the treatment of BEST1-related IRDs, including Best disease. We acquired exclusive development and commercialization rights to IC-200 through an April 2019 license agreement with Penn and UFRF. We and Penn are conducting additional preclinical studies of IC-200 and natural history studies of patients with BEST1-related IRDs. In parallel, we have engaged a gene therapy

CDMO as the manufacturer for pre-clinical and Phase 1/2 clinical supply of IC-200. Process development is ongoing and we are planning for Phase 1/2 clinical manufacturing and other IND-enabling activities. Based on current timelines and subject to regulatory review, we expect to initiate a Phase 1/2 clinical trial for IC-200 during the first half of 2021.

Minigene Therapy Research Programs

AAV vectors are generally limited as a delivery vehicle by the size of their genetic cargo, which is restricted to approximately 4,700 base pairs of genetic code. The use of "minigenes" seeks to deliver a smaller but still functional form of a larger gene packaged into a standard-size AAV delivery vector. The predominant or standard, non-mutated form of a gene is referred to as the wildtype form, and the protein resulting from expression of the wildtype gene is referred to as wildtype protein. The goal of minigene therapy is to deliver a gene expressing a protein that, although different from the wildtype protein, is nonetheless functional for purposes of treating the associated disease.

We are funding multiple sponsored research programs at the University of Massachusetts Medical School, or UMMS, seeking to use a minigene approach to develop new gene therapies for orphan IRDs. We refer to each of these programs by reference to the gene of interest for which we are seeking to create a minigene therapy. We refer to these programs collectively as our collaborative gene therapy sponsored research programs. We receive research results from these programs as they become available. UMMS has granted us an option to obtain an exclusive license to any patents or patent applications that result from these programs.

miniCEP290 Program for LCA10

One of the minigene research programs, which we refer to as the miniCEP290 program, is targeting LCA10, which is associated with mutations in the CEP290 gene. The naturally occurring CEP290 gene is approximately 8,000 base pairs. In a 2018 publication in Human Gene Therapy, researchers at UMMS presented their findings that injection of a CEP290 minigene into a newborn mouse model for LCA10 resulted in rescue of photoreceptor cells, as evidenced by both anatomical and functional measures. The goal of the sponsored research was to create and evaluate other CEP290 minigene constructs in the mouse model and optimize the effect observed in that publication.

Encouraged by the results of the sponsored research we received to date, through which we have identified what we believe are multiple promising minigene constructs, we exercised our option and in July 2019 entered into a license agreement for exclusive development and commercialization rights to patent rights and know-how for this program. The sponsored research is ongoing and UMMS is continuing to test additional CEP290 minigene constructs. We plan to continue to advance our miniCEP290 program with the constructs that appear most promising with the goal of identifying a lead product candidate in the first half of 2020 to advance into preclinical development and IND-enabling activities.

miniABCA4 Program for STGD1

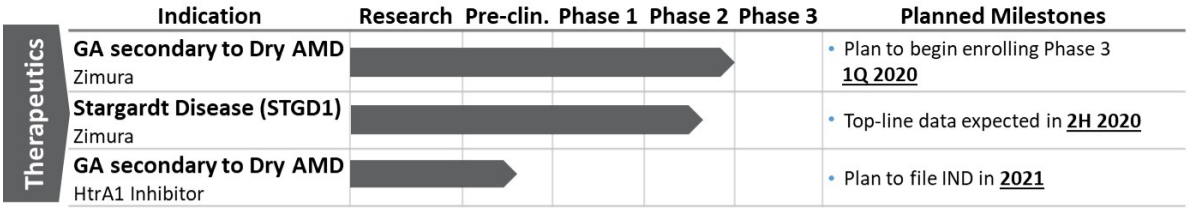
Another of the minigene research programs, which we refer to as the miniABCA4 program, is targeting STGD1, which is associated with mutations in the ABCA4 gene. UMMS is constructing and evaluating several ABCA4 minigene constructs in both in vitro and in vivo experiments. We expect to receive results from the miniABCA4 program in 2020.

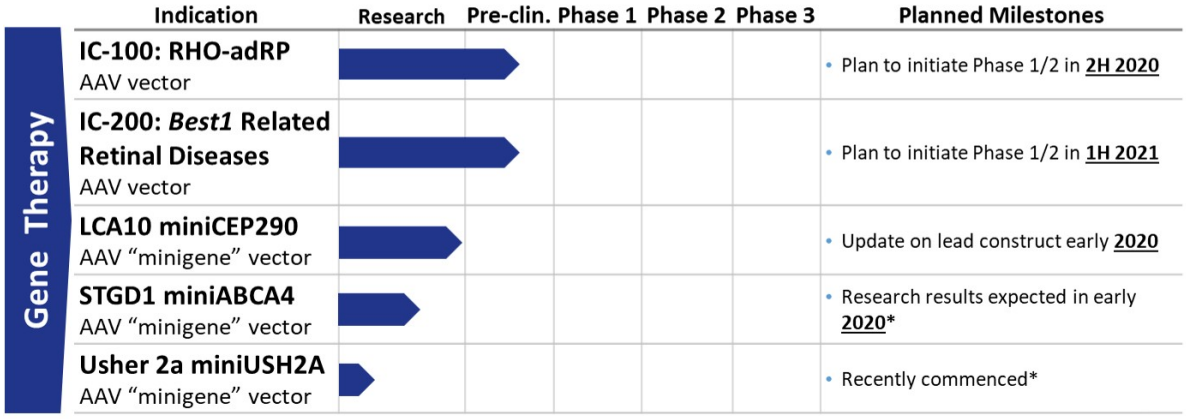
miniUSH2A Program for USH2A-Related IRDs

In July 2019, we entered into a sponsored research agreement with UMMS for USH2A-related IRDs. We refer to this program as the miniUSH2A program. This program will employ the minigene approach for the USH2A gene, which encodes a protein called usherin. Usherin is believed to be important in the development and maintenance of cells in the retina and the inner ear. Usher 2A is an autosomal recessive genetic condition characterized by hearing loss from birth and progressive vision loss, due to retinitis pigmentosa, that begins in adolescence or adulthood. USH2A-associated nonsyndromatic autosomal recessive retinitis pigmentosa is a genetic condition that manifests as vision loss without associated hearing loss. The miniUSH2A program seeks to develop an AAV deliverable, mutation independent, minigene therapy option for the vision loss associated with USH2A mutations. There are currently no U.S. Food and Drug Administration, or FDA, or European Medicines Agency, or EMA, approved therapies to treat Usher 2A or USH2A-associated nonsyndromatic autosomal recessive retinitis pigmentosa.

Research and Development Pipeline

We have summarized the current status of our ongoing research and development programs in the table below. We have given an IC number (IC-100 and IC-200) to our preclinical gene therapy product candidates. In the future, we intend to give an IC number to other gene therapy product candidates that advance to preclinical development from our collaborative gene therapy sponsored research programs or that we in-license or acquire, in each case, once a lead product candidate is identified for a particular program.





*We have an option to exclusively in-license intellectual property resulting from ongoing sponsored research.

Business Development Activities

Since early 2017, we have been pursuing a business development strategy to evaluate available technologies to treat ophthalmic diseases, particularly those in the back of the eye, and to explore opportunities to obtain rights to additional products and product candidates employing these technologies. As we evaluated numerous potential opportunities, we have come to believe that gene therapy is a promising treatment modality for retina diseases for which there are significant unmet medical needs. Our efforts have resulted in the expansion of our research and development pipeline and the transition of our company to focus principally on gene therapy. We expect to continue to evaluate, on a selective basis, opportunities to potentially obtain rights to additional gene therapy product candidates and technologies for retinal diseases. We intend to continue to focus on opportunities that present a compelling scientific rationale, have the potential to address an unmet medical need and present a meaningful commercial opportunity. To the extent feasible, we plan to target opportunities where we believe third-party funding for specific programs or technologies may be available.

In addition, based on the initial, top-line data from our OPH2003 trial of Zimura in GA, we intend to explore all options for the future development and potential commercialization of Zimura, including potential collaboration and out-licensing opportunities.

Financial Matters

As of September 30, 2019, we had cash and cash equivalents of $94.9 million. We believe that our cash and cash equivalents will be sufficient to fund our operations and capital expenditure requirements as currently planned through the first half of 2021. In addition, we reaffirm our prior estimate that year-end 2019 cash and cash equivalents will range between $80 million and $85 million. These estimates are based on our current business plan, including the continuation of our current research and development programs and the site selection and planning activities for our Phase 3 clinical trial for Zimura in GA. These estimates do not reflect any additional expenditures, including associated development costs, in the event we in-license or acquire any new product candidates or commence any new sponsored research programs. We have based these

estimates on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect.

Financial Operations Overview

Revenue

As we have no products approved for sale, we do not expect to receive any revenue related to our product candidates until we obtain regulatory approval for and commercialize such products, or until we potentially enter into agreements with third parties for the development and commercialization of our product candidates. If our development efforts for any of our product candidates result in regulatory approval or if we enter into agreements with third parties, including for any collaborations or outlicensing of rights for further development and potential commercialization of Zimura, we may generate revenue from product sales or from such third parties.

Research and Development Expenses

Our research and development expenses primarily consist of costs associated with the manufacturing, development, and preclinical and clinical testing of our product candidates and costs associated with our collaborative gene therapy sponsored research programs. Our research and development expenses consist of:

- external research and development expenses incurred under arrangements with third parties, such as academic research collaborators, contract research organizations, or CROs, and CDMOs and other vendors for the production and analysis of drug substance and drug product; and

- employee-related expenses for employees dedicated to research and development activities, including salaries, benefits and share-based compensation expense.

Research and development expenses also include costs of acquired product licenses, in-process research and development, and related technology rights where there is no alternative future use, costs of prototypes used in research and development, consultant fees and amounts paid to collaborators.

All research and development expenses are charged to operations as incurred in accordance with Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, 730, *Research and Development*, or ASC 730. We account for non-refundable advance payments for goods and services that will be used in future research and development activities as expenses when the service has been performed or when the goods have been received, rather than when the payment is made. We do not currently utilize a formal time allocation system to capture expenses on a project-by-project basis because we record expenses by functional department. Accordingly, we do not allocate all research and development expenses to individual projects or product candidates, although we do allocate some portion of these expenses by project or product candidate, as shown below.

The following table summarizes our research and development expenses for the three and nine months ended September 30, 2019 and 2018:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
	(in thousands)			
Zimura	$ 2,826	$ 5,519	$ 9,805	$ 13,255
HtrA1	150	—	382	—
IC-100: RHO-adRP	1,992	138	4,617	1,052
IC-200: BEST1-related IRDs	1,941	—	3,224	—
Other gene therapy	447	530	886	1,020
Prior product candidate Fovista	11	(391)	40	(327)
Personnel-related	1,720	1,381	5,024	4,657
Share-based compensation	942	1,171	3,101	3,717
Other	354	1,059	998	2,235
	$ 10,383	$ 9,407	$ 28,077	$ 25,609

As we continue our ongoing clinical trials for Zimura and initiate our Phase 3 clinical trial for Zimura in GA, we expect our research and development expenses for Zimura to increase. We estimate that the aggregate external costs of our Phase 3 clinical trial for Zimura in GA will range between $30 million and $40 million, depending on trial design, and that the aggregate external costs associated with manufacturing process scale-up and validation for Zimura will range between $10 million and $20 million. These costs do not include employee-related expenses for employees dedicated to Zimura clinical development and manufacturing activities, including salaries, benefits and share-based compensation expense. We also expect our research and development expenses for each of IC-100, IC-200, our miniCEP290 program and our HtrA1 inhibitors program to increase. We expect our research and development expenses for our other collaborative gene therapy sponsored research programs to decrease. Our research and development expenses may also increase if we in-license or acquire any new product candidates, including from our collaborative gene therapy sponsored research programs, or commence any new sponsored research programs.

We expect we will require substantial, additional funding in order to complete the activities necessary to develop and commercialize one or more of our product candidates. We will require additional funding as we continue the clinical development of Zimura and continue the development of our other product candidates and programs. Although the future development of our product candidates is highly uncertain, we expect the development of our product candidates will continue for at least the next several years. At this time, we cannot reasonably estimate the total remaining costs necessary to complete development, to complete process development and manufacturing scale-up and validation activities and to potentially seek marketing approval for any of our product candidates.

The successful development of our product candidates is subject to numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- the scope, rate of progress and costs of our research and development activities, including manufacturing activities;
- the potential benefits of our product candidates over other therapies;
- preclinical development results and clinical trial results;
- the terms and timing of regulatory approvals;
- our ability to market, commercialize and achieve market acceptance for any of our product candidates; and
- our ability to successfully file, prosecute, defend and enforce patent claims and other intellectual property rights, together with associated expenses.

A change in the outcome of any of these variables with respect to the development of our product candidates could mean a significant change in the costs and timing associated with the development of that product candidate.

We may require additional funding beyond what we currently expect due to unforeseen or other reasons. Our costs may exceed our expectations if we experience any unforeseen issue in our ongoing clinical trials, such as issues with the retention of enrolled patients or the availability of drug supply, or in our preclinical development programs, such as inability to develop formulations or if we experience issues with manufacturing, or if we further expand the scope of our clinical trials, preclinical development programs or collaborative gene therapy sponsored research programs. Our costs may also exceed our expectations for other reasons, for example, if we are required by the FDA, the EMA or regulatory authorities in other jurisdictions to perform clinical or nonclinical trials or other studies in addition to those we currently expect to conduct, if we experience issues with process development, establishing or scaling-up of manufacturing activities or activities to enable and qualify second source suppliers, or if we decide to increase preclinical and clinical research and development activities or build internal research capabilities or pursue internal research efforts. For example, we plan to begin a single Phase 3 clinical trial evaluating Zimura for GA with the expectation that data collected from such trial, together with data from our OPH2003 clinical trial, will be sufficient to seek marketing approval and we may subsequently decide to, or be required by regulatory authorities to, enroll additional patients in the Phase 3 clinical trial beyond our initial expectations or conduct additional clinical trials for Zimura in GA in order to seek or maintain regulatory approval. As a result of any of the above, we may need or may seek to obtain additional funding for our continuing operations sooner or in greater amounts than expected.

See the “Liquidity and Capital Resources” section of this Quarterly Report on Form 10-Q for more information regarding our current and future financial resources and our expectations regarding our research and development expenses and funding requirements.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs for personnel, including share-based compensation expense, in our executive, legal, finance, business development, human resources, investor relations and information technology functions. Other general and administrative expenses include facility costs and professional fees for legal, including patent-related, services and expenses, consulting and accounting services, and travel expenses.

Interest Income

We currently have invested our cash and cash equivalents in money market funds and investment-grade corporate debt securities, which generate a nominal amount of interest income.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with U.S. generally accepted accounting principles, or GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued research and development expenses, revenue recognition, share-based compensation and income taxes described in greater detail below. We base our estimates on our limited historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Our significant accounting policies are described in more detail in the notes to our financial statements appearing elsewhere in this Quarterly Report on Form 10-Q. Of those policies, we believe that the following accounting policies are the most critical to aid our stockholders in fully understanding and evaluating our financial condition and results of operations.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing quotations and contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses are related to expenses incurred with respect to academic research collaborators, CROs, CDMOs and other vendors in connection with research and development and manufacturing activities.

We base our expenses related to academic research collaborators, CROs and CDMOs on our estimates of the services received and efforts expended pursuant to quotations and contracts with such vendors that conduct research and development and manufacturing activities on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the applicable research and development or manufacturing expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in us reporting amounts that are too high or too low in any particular period. There have been no material changes in estimates for the periods presented.

Share-Based Compensation

We account for all share-based compensation payments issued to employees, non-employee directors, and consultants by estimating the fair value of each equity award. Accordingly, share-based compensation expense is measured based on the estimated fair value of the awards on the date of grant, net of forfeitures. We recognize compensation expense for the portion of the award that is ultimately expected to vest over the period during which the recipient renders the required services to us on a straight-line basis. In accordance with authoritative guidance, we re-measure the fair value of consultant share-based awards as the awards vest, and recognize the resulting value, if any, as expense during the period the related services are rendered.

We apply the fair value recognition provisions of ASC 718, *Compensation—Stock Compensation*. Determining the amount of share-based compensation to be recorded requires us to develop estimates of the fair value of stock options as of their grant date. We recognize share-based compensation expense ratably over the requisite service period, which in most cases is the vesting period of the award. For grants containing performance-based vesting provisions, expense is recognized over the estimated achievement period only when the performance-based milestone is deemed probable of achievement. If performance-based milestones are later determined not to be probable of achievement, then all previously recorded stock-based compensation expense associated with such options will be reversed during the period in which we make this determination. Calculating the fair value of share-based awards requires us to make highly subjective assumptions.

Prior to January 1, 2019, share-based compensation awarded to non-employees was subject to revaluation over the vesting term of each award. Subsequent to the adoption of ASU 2018-07, *Improvements to Non-Employee Share-Based Payment Accounting*, the value of non-employee share-based compensation is measured on the date of grant, similar to share-based compensation granted to employees.

We use the Black-Scholes option pricing model to value our stock option awards and the options to purchase shares under our employee stock purchase plan. Use of this valuation methodology requires that we make assumptions as to: the volatility of our common stock, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options and the expected dividend yield of our common stock. As a recent public company, we do not have sufficient history to estimate the volatility of our common stock price or the expected life of the options. We calculate expected volatility based on reported data for similar publicly traded companies for which historical information is available and will continue to do so until the historical volatility of our common stock is sufficient to measure expected volatility for future option grants.

We use the simplified method as prescribed by the Securities and Exchange Commission Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term of stock option grants to employees as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees. The risk-free interest rate used for each grant is based on the U.S. Treasury yield curve in effect at the time of grant for instruments with a similar expected life. We utilize a dividend yield of zero based on the fact that we have never paid cash dividends and have no current intention to pay cash dividends. The weighted-average assumptions used to estimate grant date fair value of stock options using the Black-Scholes option pricing model were as follows for the three and nine months ended September 30, 2019 and 2018:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Expected common stock price volatility	89%	84%	88%	83%
Risk-free interest rate	1.38%-1.84%	2.80%-2.90%	1.38%-2.54%	2.39%-2.90%
Expected term of options (years)	6.1	6.1	5.7	5.8
Expected dividend yield	—	—	—	—

We estimate the fair value of restricted stock units, or RSUs, granted to employees using the closing market price of our common stock on the date of grant.

We also estimate forfeitures at the time of grant and revise those estimates in subsequent periods if actual forfeitures differ from our estimates. We use historical data to estimate pre-vesting forfeitures and record share-based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from our estimates, the difference is recorded as a cumulative adjustment in the period the estimates were revised.

Share-based compensation expense for equity grants to employees, non-employee directors and consultants was $2.1 million and $2.6 million for the three months ended September 30, 2019 and 2018, respectively, net of expected forfeitures. Share-based compensation expense for equity grants to employees, non-employee directors and consultants was $6.8 million and $8.3 million for the nine months ended September 30, 2019 and 2018, respectively, net of expected forfeitures.

As of September 30, 2019, we had $6.5 million of total unrecognized share-based compensation expense, which we expect to recognize over a weighted-average remaining vesting period of approximately 1.6 years. We expect our share-based compensation expense for our equity awards to employees, non-employee directors and consultants to decrease in future periods as a result of a decrease in the fair value of our common stock.

For the three and nine months ended September 30, 2019 and 2018, we allocated share-based compensation as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
	(in thousands)			
Research and development	$ 942	$ 1,171	$ 3,101	$ 3,717
General and administrative	1,184	1,433	3,702	4,631
Total	$ 2,126	$ 2,604	$ 6,803	$ 8,348

In October 2019, our board of directors adopted the 2019 Inducement Stock Incentive Plan, or the Inducement Plan, pursuant to which we may grant, subject to the terms of the Inducement Plan and Nasdaq rules, nonstatutory stock options, restricted stock, restricted stock units, and other stock-based awards up to an aggregate of 1,000,000 shares of our common stock. The Inducement Plan permits us to, subject to the approval of each grant by the compensation committee of our board of directors, use the stock-based awards available under the Inducement Plan to attract key employees for the growth of our business. On October 31, 2019, we filed a Registration Statement on Form S-8 with the Securities and Exchange Commission, or the SEC, to register under the Securities Act of 1933, as amended, all shares that are issuable under the Inducement Plan. An initial award under the Inducement Plan consisting of an option to purchase 300,000 shares of our common stock and 50,000 restricted stock units was granted to one new employee and effective as of November 1, 2019.

Income Taxes

For the three and nine months ended September 30, 2019, we recorded a $0.1 million benefit for income taxes. For the three and nine months ended September 30, 2018, we recorded a de minimis provision for income taxes and a $0.8 million benefit for income taxes, respectively. The income tax benefit for the three and nine months ended September 30, 2019 was primarily to reflect a settlement of a local tax audit. The benefit for income taxes recorded during the nine months ended September 30, 2018 includes the settlement of a local tax audit recorded during the three months ended June 30, 2018 offset partially by the provision for income taxes recorded during the three months ended March 31, 2018 to reflect the impact of sequestration on our estimate of refundable AMT credits.

The deferred tax assets associated with our losses incurred in 2018 and to date in 2019 have a full valuation allowance recorded against them due to our history of losses and the lack of other positive evidence to support future taxable income against which these losses could be applied. See Note 6 to our financial statements in Part I-Item 1 of this Quarterly Report on Form 10-Q for further information regarding our expectations with respect to our income tax provision.

Results of Operations

Comparison of Three Month Periods Ended September 30, 2019 and 2018

	Three months ended September 30,		Increase (Decrease)
	2019	2018	
	(in thousands)		
Statements of Operations Data:			
Operating expenses:			
Research and development	$ 10,383	$ 9,407	$ 976
General and administrative	4,674	5,968	(1,294)
Total operating expenses	15,057	15,375	(318)
Loss from operations	(15,057)	(15,375)	(318)
Interest income	495	637	(142)
Other income (expense)	—	(1)	(1)
Loss before income tax provision (benefit)	(14,562)	(14,739)	(177)
Income tax provision (benefit)	(125)	6	(131)
Net loss	$ (14,437)	$ (14,745)	$ (308)

Research and Development Expenses

Our research and development expenses were $10.4 million for the three months ended September 30, 2019, an increase of $1.0 million compared to $9.4 million for the three months ended September 30, 2018. The increase in research and development expenses for the three months ended September 30, 2019 was primarily due to a $3.7 million increase in costs resulting from the initiation and expansion of our gene therapy programs and a $0.2 million increase in costs resulting from the initiation of our HtrA1 inhibitor program. This increase was offset by a $2.7 million decrease in costs associated with our Zimura programs. The decreased costs for our Zimura programs included lower costs related to a decrease in Zimura manufacturing activities and lower clinical trial costs as a result of the completion of the OPH2007 wet AMD trial during the fourth quarter of 2018 and the completion of patient recruitment for our OPH2003 dry AMD trial during the fourth quarter of 2018 and the associated reduction in site initiation costs.

General and Administrative Expenses

Our general and administrative expenses were $4.7 million for the three months ended September 30, 2019, a decrease of $1.3 million, compared to $6.0 million for the three months ended September 30, 2018. The decrease in general and administrative expenses for the three months ended September 30, 2019 was primarily due to a decrease in costs to support our operations and infrastructure.

Interest Income

Interest income for the three months ended September 30, 2019 was $0.5 million compared to interest income of $0.6 million for the three months ended September 30, 2018.

Income Tax Provision (Benefit)

For the three months ended September 30, 2019, we recorded an income tax benefit which was primarily to reflect a settlement of a local tax audit. For the three months ended September 30, 2018, we recorded a de minimis provision for income taxes.

Comparison of Nine Month Periods Ended September 30, 2019 and 2018

	Nine months ended September 30,		
	2019	2018	Increase (Decrease)
	(in thousands)		
Statements of Operations Data:			
Operating expenses:			
Research and development	$ 28,077	$ 25,609	$ 2,468
General and administrative	15,353	17,945	(2,592)
Total operating expenses	43,430	43,554	(124)
Loss from operations	(43,430)	(43,554)	(124)
Interest income	1,782	1,711	71
Other income (expense)	151	(17)	(168)
Loss before income tax provision (benefit)	(41,497)	(41,860)	(363)
Income tax benefit	(116)	(833)	(717)
Net loss	$ (41,381)	$ (41,027)	$ 354

Research and Development Expenses

Our research and development expenses were $28.1 million for the nine months ended September 30, 2019, an increase of $2.5 million compared to $25.6 million for the nine months ended September 30, 2018. The increase in research and development expenses for the nine months ended September 30, 2019 was primarily due to a $6.7 million increase in costs resulting from the initiation and expansion of our gene therapy programs and a $0.4 million increase in costs resulting from the initiation of our HtrA1 inhibitor program. This increase was offset by a $3.5 million decrease in costs associated with our Zimura programs and a $1.2 million decrease in professional and consulting fees. The decreased costs for our Zimura programs included lower costs related to a decrease in Zimura manufacturing activities and lower clinical trial costs as a result of the completion of the OPH2007 wet AMD trial during the fourth quarter of 2018 and the completion of patient recruitment for our OPH2003 dry AMD trial during the fourth quarter of 2018 and the associated reduction in site initiation costs.

General and Administrative Expenses

Our general and administrative expenses were $15.4 million for the nine months ended September 30, 2019, a decrease of $2.6 million, compared to $17.9 million for the nine months ended September 30, 2018. The decrease in general and administrative expenses for the nine months ended September 30, 2019 was primarily due to a decrease in costs to support our operations and infrastructure.

Interest Income

Interest income for the nine months ended September 30, 2019 was $1.8 million compared to interest income of $1.7 million for the nine months ended September 30, 2018. The increase in interest income was the result of an increase in interest rates and a change in the mix of our investment portfolio, which previously only included investments in money market funds and now includes investment in certain investment-grade corporate debt securities with original maturities of 90 days or less, partially offset by a decrease in cash balances available for investment.

Income Tax Benefit

We recorded an income tax benefit of $0.1 million and $0.8 million for the nine months ended September 30, 2019 and 2018, respectively. For the nine months ended September 30, 2019, the Company recorded a benefit for income taxes primarily to reflect a settlement of a local tax audit. The benefit for income taxes recorded during the nine months ended September 30, 2018 includes the settlement of a local tax audit recorded by the Company during the three months ended June 30, 2018 offset partially by the provision for income taxes recorded by the Company during the three months ended March 31, 2018 to reflect the impact of sequestration on the Company's estimate of refundable AMT credits.

Liquidity and Capital Resources

Sources of Liquidity

Since inception, we have financed our operations primarily through private placements of our preferred stock, venture debt borrowings, funding we received under our prior Fovista royalty purchase and sale agreement with Novo Holdings A/S, our initial public offering of common stock, which we closed in September 2013, our follow-on public offering of common stock, which we closed in February 2014, funds we received under a prior Fovista licensing and commercialization agreement with Novartis Pharma AG, and the approximately $6.1 million in cash that we received in connection with our acquisition of Inception 4 in October 2018. We do not have any committed external source of funds.

We currently have an effective universal shelf registration statement on Form S-3 on file with the SEC registering for sale from time to time up to $150.0 million of common stock, preferred stock, debt securities, depositary shares, warrants and/or units in one or more registered offerings, of which $50.0 million may be offered, issued and sold under an “at-the-market” Sales Agreement, or the ATM Agreement, with Cowen and Company, LLC. We have not yet issued and sold any shares of our common stock under the ATM Agreement.

Cash Flows

As of September 30, 2019, we had cash and cash equivalents totaling $94.9 million and no debt. We currently have invested our cash and cash equivalents in money market funds and certain investment-grade corporate debt securities with original maturities of 90 days or less.

The following table shows a summary of our cash flows for the nine months ended September 30, 2019 and 2018:

	Nine months ended September 30,	
	2019	2018
	(in thousands)	
Net cash (used in) provided by:		
Operating Activities	$ (36,581)	$ (31,829)
Investing Activities	150	—
Financing Activities	81	65
Net change in cash and cash equivalents	$ (36,350)	$ (31,764)

Cash Flows from Operating Activities

Net cash used in operating activities in the nine months ended September 30, 2019 related primarily to net cash used to fund our research and development activities for Zimura, IC-100 and IC-200 and our collaborative gene therapy sponsored research programs and to support our general and administrative operations. Net cash used in operating activities in the nine months ended September 30, 2018 related primarily to net cash used to fund our research and development activities for Zimura and to support our general and administrative operations.

See "—Funding Requirements" below for a description of how we expect to use our cash for operating activities in future periods.

Cash Flows from Investing Activities

Net cash provided by investing activities for the nine months ended September 30, 2019 related to the proceeds received from the sale of manufacturing and clinical equipment. We had no net cash provided by investing activities for the nine months ended September 30, 2018.

Cash Flows from Financing Activities

Net cash provided by financing activities for the nine months ended September 30, 2019 and 2018 related to purchases made under our employee stock purchase plan.

Funding Requirements

Zimura is in clinical development, our gene therapy product candidates IC-100 and IC-200 and our HtrA1 inhibitor program are each in preclinical development, and we are funding multiple ongoing collaborative gene therapy sponsored research programs. We expect our research and development expenses to increase as we pursue these programs as currently planned and as we initiate our Phase 3 clinical trial for Zimura in GA. For example, we estimate that the aggregate external

costs of our Phase 3 clinical trial for Zimura in GA will range between $30 million and $40 million, depending on trial design, and that the aggregate external costs associated with manufacturing process scale-up and validation for Zimura will range between $10 million and $20 million. These costs do not include employee-related expenses for employees dedicated to Zimura clinical development and manufacturing activities, including salaries, benefits and share-based compensation expense. Our estimates could change in the event that we modify the design of our Phase 3 clinical trial for Zimura in GA, if we decide or are required to conduct one or more additional clinical trials of Zimura in GA beyond our currently planned Phase 3 clinical trial in order to obtain data sufficient to seek regulatory approval in this indication or for other reasons, if we encounter difficulties in Zimura manufacturing scale-up and process validation, or if we encounter delays or other unforeseen events. We could also incur additional research and development expenses as we evaluate and potentially in-license or acquire, and undertake development of, additional product candidates, including any promising product candidates that emerge from our collaborative gene therapy sponsored research programs. Furthermore, if we successfully develop and obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. We are party to agreements with Archemix Corp. with respect to Zimura, UFRF and Penn with respect to IC-100 and IC-200, UMMS with respect to any potential product candidates from our miniCEP290 program, and the former equityholders of Inception 4 with respect to our HtrA1 inhibitor program, in each case, that impose significant milestone payment obligations on us if we achieve specified clinical, regulatory and commercial milestones with respect to these product candidates or programs, as well as certain royalties on net sales with respect to IC-100, IC-200 and any product candidates we choose to develop from our miniCEP290 program. It is likely that any future in-licensing or acquisition agreements that we enter into with respect to additional product candidates or technologies would include similar obligations.

We expect that we will continue to incur significant expenses as we:

- continue the clinical development of Zimura in GA and STGD1;
- continue the development of IC-100 and IC-200 and pursue our collaborative gene therapy sponsored research programs;
- continue the preclinical development of our HtrA1 inhibitor program;
- in-license or acquire the rights to, and pursue the development of, other product candidates or technologies;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, manufacturing, quality control, quality assurance and scientific personnel;
- seek marketing approval for any product candidates that successfully complete clinical trials;
- expand our outsourced manufacturing activities or establish commercial operations or sales, marketing and distribution capabilities, if we receive, or expect to receive, marketing approval for any of our product candidates; and
- expand our general and administrative functions to support our future growth.

As of September 30, 2019, we had cash and cash equivalents of $94.9 million. We believe that our cash and cash equivalents will be sufficient to fund our operations and capital expenditure requirements as currently planned through the first half of 2021. In addition, we reaffirm our prior estimate that year-end 2019 cash and cash equivalents will range between $80 million and $85 million. These estimates are based on our current business plan, including the continuation of our current research and development programs and the site selection and planning activities for our Phase 3 clinical trial for Zimura in GA. These estimates do not reflect any additional expenditures, including associated development costs, in the event we in-license or acquire any new product candidates or commence any new sponsored research programs. We have based these estimates on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect.

We expect we will require substantial, additional funding in order to complete the activities necessary to develop and commercialize one or more of our product candidates. We will require additional funding as we continue the clinical development of Zimura and continue the development of our other product candidates and programs. Although the future development of our product candidates is highly uncertain, we expect the development of our product candidates will continue for at least the next several years. At this time, we cannot reasonably estimate the total remaining costs necessary to complete development, to complete process development and manufacturing scale-up and validation activities and to potentially seek marketing approval for any of our product candidates.

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

- the scope, progress, costs and results of our Zimura clinical programs, as well as our ability to secure external funding for any additional internal development we may undertake to obtain data sufficient to seek marketing approval for Zimura in GA or any other indication;
- the scope, progress, costs and results of our efforts to develop IC-100 and IC-200, including activities to establish manufacturing capabilities and preclinical testing to enable us to file investigational new drug applications, or INDs, for these product candidates;
- the scope, progress, costs and results from our collaborative gene therapy sponsored research programs, including costs related to the in-license and future development of any promising product candidates and technologies that emerge from these programs;
- the scope, progress, costs and results of our efforts to develop our HtrA1 inhibitor program, including formulation development and other preclinical development activities;
- the costs, progress and timing of process development, manufacturing scale-up and validation activities, analytical development and stability studies associated with our product candidates;
- the extent to which we in-license or acquire rights to, and undertake research or development of, additional product candidates or technologies;
- our ability to establish collaborations on favorable terms, if at all, if we choose to do so, including any collaboration for the further clinical development and potential commercialization of Zimura;
- the costs, timing and outcome of regulatory filings and reviews of our product candidates;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending intellectual property-related claims;
- the timing, scope and cost of commercialization activities for any of our product candidates if we receive, or expect to receive, marketing approval for a product candidate; and
- subject to receipt of marketing approval, net revenue received from commercial sales of any of our product candidates, after milestone payments and royalty payments that we would be obligated to make.

We do not have any committed external source of funds. Our ability to raise adequate additional financing when needed, and on terms acceptable to us, will depend on many factors. These factors include investors' perceptions of the potential success of our ongoing business, including the development of our product candidates and other programs, and the potential future growth of our business. Additionally, these factors include general market conditions that also affect other companies. These factors may make raising capital difficult, and may result in us accepting terms that are unfavorable to us, especially if we are in need of financing at the particular time. The size of our company and our status as a company listed on The Nasdaq Stock Market, or Nasdaq, may also limit our ability to raise financing. For example, our ability to raise adequate financing through a public offering may be limited by market conditions and SEC rules based on our current market capitalization. Nasdaq listing rules also generally limit the number of shares we may issue in a private placement to a number less than 20% of the number of shares of our common stock outstanding immediately prior to the transaction, unless we issue such shares at a premium, which investors may be unwilling to accept, or unless we obtain shareholder approval, which can be expensive and time-consuming and can add risk to our ability to complete the financing transaction. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate the development of our product candidates, our collaborative gene therapy sponsored research programs, or our future commercialization efforts.

Until such time, if ever, when we can generate substantial product revenues, we may need or may seek to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, our existing stockholders' ownership interests would be diluted, and the terms of these new securities may include liquidation or other preferences that adversely affect our existing stockholders' rights as common stockholders. The dilutive effect of future capital raises may be substantial, depending on the price of our common stock at the time of such capital raise, with a lower stock price translating to greater dilution for existing stockholders. Debt financing and preferred equity 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. In addition, we have issued, and may in the future issue additional, equity securities as consideration for business development transactions, which may also dilute our existing stockholders' ownership interests.

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, products or product candidates or 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 grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

Our need for additional financing may continue even if we are able to successfully develop one or more of our product candidates. Our future commercial revenues, if any, will be derived from sales of such product candidates, which may not be available for at least several years following completion of successful product development, if at all. In addition, if approved, our product candidates may not achieve commercial success. Even if those products are successful and we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Under most, if not all, of the foregoing circumstances, we may need to obtain substantial additional financing to achieve our business objectives.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of September 30, 2019:

	Payments Due by Period				
	Total	Less than 1 year	1 - 3 years	3 - 5 years	More than 5 years
	(in thousands)				
Sponsored Research (1)	$ 2,154	$ 2,088	$ 66	$ —	$ —
Operating Leases (2)	764	764	—	—	—
Total (3)	$ 2,918	$ 2,852	$ 66	$ —	$ —

(1) The table above includes our contracted obligations under our sponsored research agreements.

(2) The table above includes our continuing rent obligations through June 2020, which is when our lease at One Penn Plaza is currently scheduled to expire.

(3) This table does not include:

- any milestone payments which may become payable to third parties under license or acquisition agreements as the timing and likelihood of such payments are not known with certainty;
- any royalty payments to third parties as the amounts, timing and likelihood of such payments are not known;
- anticipated expenditures under supply agreements for periods for which we are not yet bound under binding purchase orders; or
- contracts that are entered into in the ordinary course of business that are not material in the aggregate in any period presented above.

In addition to the amounts set forth in the table above, we may be required, under the agreements under which we acquired rights to our product candidates, to make milestone payments and/or pay royalties. For example, based on the initial, top-line data from our OPH2003 trial of Zimura in GA, we are obligated, under the license agreement to which we obtained rights to Zimura, to pay Archemix Corp. a milestone payment of $1.0 million during the first quarter of 2020. This payment and other payments for Zimura, IC-100, IC-200, any product candidates we may develop from our miniCEP290 program and our HtrA1 program are described in "Note 9—Commitments and Contingencies" and "Note 10—Subsequent Events" in our unaudited consolidated financial statements appearing elsewhere in this Quarterly Report.

We also have letter agreements with certain employees that require the funding of a specific level of payments if certain events, such as a termination of employment in connection with a change in control or termination of employment by the employee for good reason or by us without cause, occur. For a description of these obligations, see our definitive proxy statement on Schedule 14A for our 2019 annual meeting of stockholders, as filed with the SEC on April 18, 2019.

In addition, in the course of normal business operations, we have agreements with contract service providers to assist in the performance of our research and development and manufacturing activities. Expenditures to CROs and CDMOs represent significant costs in preclinical and clinical development. Subject to required notice periods and our obligations under binding purchase orders and any cancellation fees that we may be obligated to pay, we can elect to discontinue the work under these agreements at any time. We may also enter into additional collaborative research, contract research, manufacturing, and supplier agreements in the future, which may require upfront payments and even long-term commitments of cash.

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 Securities and Exchange Commission rules.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risk related to changes in interest rates. We had cash and cash equivalents of $94.9 million as of September 30, 2019, consisting of cash and investments in money market funds and certain investment-grade corporate debt securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because a significant portion of our investments are in short-term securities. Due to the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

We contract with CROs and certain other vendors to perform services outside of the United States. We may be subject to fluctuations in foreign currency rates in connection with certain of these agreements. Transactions denominated in currencies other than the U.S. dollar are recorded based on exchange rates at the time such transactions arise. As of September 30, 2019, substantially all of our total liabilities were denominated in the U.S. dollar.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our chief executive officer and chief financial officer, evaluated the effectiveness of our disclosure controls and procedures as of September 30, 2019. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or 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 is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, 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 management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Based on the evaluation of our disclosure controls and procedures as of September 30, 2019, our chief executive officer and chief financial officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control Over Financial Reporting

No changes in our internal control over financial reporting (as defined in Rules 13a-15(d) and 15d-15(d) under the Exchange Act) occurred during the quarter ended September 30, 2019 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II

Item 1. Legal Proceedings

On January 11, 2017, a putative class action lawsuit was filed against us and certain of our current and former executive officers in the United States District Court for the Southern District of New York, captioned Frank Micholle v. Ophthotech Corporation, et al., No. 1:17-cv-00210. On March 9, 2017, a related putative class action lawsuit was filed against us and the same group of our current and former executive officers in the United States District Court for the Southern District of New York, captioned Wasson v. Ophthotech Corporation, et al., No. 1:17-cv-01758. These cases were consolidated on March 13, 2018. On June 4, 2018, the lead plaintiff filed a consolidated amended complaint, the CAC. The CAC purports to be brought on behalf of shareholders who purchased our common stock between March 2, 2015 and December 12, 2016. The CAC generally alleges that we and certain of our officers violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning the results of our Phase 2b trial and the prospects of our Phase 3 trials for Fovista in combination with anti-VEGF agents for the treatment of wet AMD. The CAC seeks unspecified damages, attorneys' fees, and other costs. We and the individual defendants filed a motion to dismiss the CAC on July 27, 2018. On September 18, 2019, the court issued an order dismissing some, but not all, of the allegations in the CAC.

On February 7, 2018, a shareholder derivative action was filed against the members of our board of directors in the New York Supreme Court Commercial Division, captioned Cano v. Guyer, et al., No. 650601/2018. The complaint alleges that the defendants breached their fiduciary duties to our company by adopting a compensation plan that overcompensates the non-employee members of our board of directors relative to boards of directors of companies of comparable market capitalization and size. The complaint also alleges that the defendants were unjustly enriched as a result of the alleged conduct. The complaint purports to seek unspecified damages on our behalf, attorneys' fees, and other costs, as well as an order directing us to reform and improve our corporate governance and internal procedures to comply with applicable laws. We filed a motion to dismiss this case on May 14, 2018. On June 4, 2018, the plaintiff filed an amended complaint. On June 25, 2018, we filed a renewed motion to dismiss this case. On December 3, 2018, the parties filed a stipulation of settlement that contemplates that we will adopt certain compensation-related governance reforms and does not obligate the defendants or us to pay any monetary damages. The court approved the settlement at a hearing on March 12, 2019. As part of the settlement, in April 2019 we paid $300,000 in fees and costs to plaintiff's counsel. As contemplated by the settlement, our board adopted certain compensation-related governance reforms, including a non-employee director compensation policy, which our stockholders approved on May 15, 2019 at our 2019 annual meeting.

On August 31, 2018, a shareholder derivative action was filed against current and former members of our board of directors and certain of our current and former officers in the United States District Court for the Southern District of New York, captioned Luis Pacheco v. David R. Guyer, et al., Case No. 1:18-cv-07999. The complaint, which is based substantially on the facts alleged in the CAC, alleges that the defendants breached their fiduciary duties to our company and wasted our corporate assets by failing to oversee our business, and also alleges that the defendants were unjustly enriched as a result of the alleged conduct, including through receipt of bonuses, stock options and similar compensation from us, and through sales of our stock between March 2, 2015 and December 12, 2016. The complaint purports to seek unspecified damages on our behalf, attorneys' fees, and other costs, as well as an order directing us to reform and improve our corporate governance and internal procedures to comply with applicable laws, including submitting certain proposed amendments to our corporate charter, bylaws and corporate governance policies for vote by our stockholders. On December 14, 2018, we filed a motion to dismiss the complaint. On September 19, 2019, the court denied our motion to dismiss this complaint. This matter was subsequently referred to a special litigation committee of our board of directors.

On October 16, 2018, our board of directors received a shareholder demand to investigate and commence legal proceedings against certain members of our board of directors. The demand alleges facts that are substantially similar to the facts alleged in the CAC and the Pacheco complaint and asserts claims that are substantially similar to the claims asserted in the Pacheco complaint. On January 30, 2019, our board of directors received a second shareholder demand from a different shareholder to investigate and commence legal proceedings against certain current and former members of our board of directors based on allegations that are substantially similar to the allegations contained in the first demand letter. These shareholder demands have been referred to a demand review committee of our board of directors.

We deny any and all allegations of wrongdoing and intend to vigorously defend against these lawsuits. We are unable, however, to predict the outcome of these matters at this time. Moreover, any conclusion of these matters in a manner adverse to us and for which we incur substantial costs or damages not covered by our directors' and officers' liability insurance would have a material adverse effect on our financial condition and business. In addition, the litigation could adversely impact our reputation and divert management's attention and resources from other priorities, including the execution of our business plan

and strategies that are important to our ability to grow our business, any of which could have a material adverse effect on our business.

Item 1A. Risk Factors

The following risk factors and other information included in this Quarterly Report on Form 10-Q should be carefully considered. The risks and uncertainties described below are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 1 of this Quarterly Report on Form 10-Q for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to Our Business Plan, Financial Position and Need for Additional Capital

We are a development-stage company without any commercial products. The value of our company, therefore, is highly dependent on the success of our research and development efforts and the amount of our available cash. Our research and development programs, which are focused on novel therapies and technologies, carry significant scientific and other risks. If any of these programs are not successful, the value of your investment may decline.

We are a development-stage company without any approved products. Our growth prospects and the future value of our company are highly dependent on the progress of our research and development programs, including our ongoing and any future clinical trials for Zimura, our preclinical development programs for IC-100 and IC-200, our collaborative gene therapy sponsored research programs, and our preclinical development program for our HtrA1 inhibitors. Drug development is a highly uncertain undertaking and carries significant scientific and other risks.

We may encounter unforeseen difficulties, complications, delays, expenses and other known and unknown factors. We may never be successful in developing or commercializing any of our product candidates or other programs. There is a high rate of failure in pharmaceutical research and development. Even if we have promising preclinical or clinical candidates, their development could fail at any time. Our failure could be due to unexpected scientific, safety or efficacy issues with our product candidates and other programs, invalid hypotheses regarding the molecular targets and mechanisms of action we choose to pursue or unexpected delays in our research and development programs resulting from applying the wrong criteria or experimental systems and procedures to our programs or lack of experience, with the possible result that none of our product candidates or other programs result in the development of marketable products. We have not yet demonstrated our ability to successfully complete the development of a pharmaceutical product, including completion of large-scale, pivotal clinical trials with safety and efficacy data sufficient to obtain marketing approval or activities necessary to apply for and obtain marketing approval, including the qualification of a commercial manufacturer through a pre-approval inspection with regulatory authorities. If successful in developing and obtaining marketing approval of one of our product candidates, we would 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, as our company has never conducted the sales, marketing and distribution activities necessary for successful product commercialization.

Because the value of our company is largely based on the prospects for our research and development programs and their potential to result in therapies capable of achieving marketing approval and generating future revenues, any failure, delay or setback for these programs will likely have a negative impact on the value of your investment. In addition, because a number of our product candidates are in an early, preclinical stage, even if we are successful in advancing the research and development of those product candidates, the value of our common stock may not rise in a meaningful way, which could affect our ability to raise additional finances. As we continue to invest in these research and development programs to generate data to support further development, the amount of our available cash will continue to decline until we raise additional finances.

We have a history of significant operating losses. We expect to continue to incur losses until such time, if ever, that we successfully commercialize our product candidates and may never achieve or maintain profitability.

Since inception, we have experienced significant cash outflows in funding our operations. To date, we have not generated any revenues from commercial product sales and have financed our operations primarily through private placements of our preferred stock, venture debt borrowings, funds received under our prior Fovista royalty purchase and sale agreement with Novo Holdings A/S, our initial public offering, which we closed in September 2013, our follow-on public offering, which we closed in February 2014, funds we received under our prior Fovista licensing and commercialization agreement with Novartis Pharma AG, and funds we received in connection with our acquisition of Inception 4 in October 2018. As of September 30, 2019, we had an accumulated deficit of $463.0 million. Our net loss was $41.4 million for the nine months ended September 30, 2019 and we expect to continue to incur significant operating losses for the foreseeable future.

Zimura is in clinical development, our gene therapy product candidates IC-100 and IC-200 and our HtrA1 inhibitor program are each in preclinical development, and we are funding multiple ongoing collaborative gene therapy sponsored research programs. We expect our research and development expenses to increase as we pursue these programs as currently planned and as we initiate our Phase 3 clinical trial for Zimura in GA. For example, we estimate that the aggregate external costs of our Phase 3 clinical trial for Zimura in GA will range between $30 million and $40 million, depending on trial design, and that the aggregate external costs associated with manufacturing process scale-up and validation for Zimura will range between $10 million and $20 million. These costs do not include employee-related expenses for employees dedicated to Zimura clinical development and manufacturing activities, including salaries, benefits and share-based compensation expense. Our estimates could change in the event that we modify the design of our Phase 3 clinical trial for Zimura in GA, if we decide or are required to conduct one or more additional clinical trials of Zimura in GA beyond our currently planned Phase 3 clinical trial in order to obtain data sufficient to seek regulatory approval in this indication or for other reasons, if we encounter difficulties in Zimura manufacturing scale-up and process validation, or if we encounter delays or other unforeseen events. We could also incur additional research and development expenses as we evaluate and potentially in-license or acquire, and undertake development of, additional product candidates, including any promising product candidates that emerge from our collaborative gene therapy sponsored research programs. Furthermore, if we successfully develop and obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. We are party to agreements with Archemix Corp. with respect to Zimura, UFRF and Penn with respect to IC-100 and IC-200, UMMS with respect to any potential product candidates from our miniCEP290 program, and the former equityholders of Inception 4 with respect to our HtrA1 inhibitor program, in each case, that impose significant milestone payment obligations on us if we achieve specified clinical, regulatory and commercial milestones with respect to these product candidates or programs, as well as certain royalties on net sales with respect to IC-100, IC-200 and any product candidates we choose to develop from our miniCEP290 program. It is likely that any future in-licensing or acquisition agreements that we enter into with respect to additional product candidates or technologies would include similar obligations.

We expect that we will continue to incur significant expenses as we:

- continue the clinical development of Zimura in GA and STGD1;
- continue the development of IC-100 and IC-200 and pursue our collaborative gene therapy sponsored research programs;
- continue the preclinical development of our HtrA1 inhibitor program;
- in-license or acquire the rights to, and pursue the development of, other product candidates or technologies;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, manufacturing, quality control, quality assurance and scientific personnel;
- seek marketing approval for any product candidates that successfully complete clinical trials;
- expand our outsourced manufacturing activities or establish commercial operations or sales, marketing and distribution capabilities, if we receive, or expect to receive, marketing approval for any of our product candidates; and
- expand our general and administrative functions to support our future growth.

Our ability to become and remain profitable depends on our ability to generate revenue in excess of our expenses. Our ability to generate revenues from product sales is dependent on our obtaining marketing approval for and commercializing our product candidates or any product candidates we may in-license or acquire. We may be unsuccessful in our efforts to develop and commercialize product candidates or in our efforts to in-license or acquire additional product candidates. Even if we succeed in developing and commercializing one or more of our product candidates, we may never achieve sufficient sales revenue to achieve or maintain profitability. See “—Risks Related to Product Development and Commercialization” for a further discussion of the risks we face in successfully developing and commercializing our product candidates and achieving profitability.

We expect we will require substantial, additional funding in order to complete the activities necessary to develop and commercialize one or more of our product candidates. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts. We may require additional funding beyond what we currently expect or sooner than we currently expect.

As of September 30, 2019, we had cash and cash equivalents of $94.9 million. We believe that our cash and cash equivalents will be sufficient to fund our operations and capital expenditure requirements as currently planned through the first

half of 2021. In addition, we reaffirm our prior estimate that year-end 2019 cash and cash equivalents will range between $80 million and $85 million. These estimates are based on our current business plan, including the continuation of our current research and development programs and the site selection and planning activities for our Phase 3 clinical trial for Zimura in GA. These estimates do not reflect any additional expenditures, including associated development costs, in the event we in-license or acquire any new product candidates or commence any new sponsored research programs. We have based these estimates on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect.

We expect we will require substantial, additional funding in order to complete the activities necessary to develop and commercialize one or more of our product candidates. We will require additional funding as we continue the clinical development of Zimura and continue the development of our other product candidates and programs. Although the future development of our product candidates is highly uncertain, we expect the development of our product candidates will continue for at least the next several years. At this time, we cannot reasonably estimate the total remaining costs necessary to complete development, to complete process development and manufacturing scale-up and validation activities and to potentially seek marketing approval for any of our product candidates.

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

- the scope, progress, costs and results of our Zimura clinical programs, as well as our ability to secure external funding for any additional internal development we may undertake to obtain data sufficient to seek marketing approval for Zimura in GA or any other indication;
- the scope, progress, costs and results of our efforts to develop IC-100 and IC-200, including activities to establish manufacturing capabilities and preclinical testing to enable us to file investigational new drug applications, or INDs, for these product candidates;
- the scope, progress, costs and results from our collaborative gene therapy sponsored research programs, including costs related to the in-license and future development of any promising product candidates and technologies that emerge from these programs;
- the scope, progress, costs and results of our efforts to develop our HtrA1 inhibitor program, including formulation development and other preclinical development activities;
- the costs, progress and timing of process development, manufacturing scale-up and validation activities, analytical development and stability studies associated with our product candidates;
- the extent to which we in-license or acquire rights to, and undertake research or development of, additional product candidates or technologies;
- our ability to establish collaborations on favorable terms, if at all, if we choose to do so, including any collaboration for the further clinical development and potential commercialization of Zimura;
- the costs, timing and outcome of regulatory filings and reviews of our product candidates;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending intellectual property-related claims;
- the timing, scope and cost of commercialization activities for any of our product candidates if we receive, or expect to receive, marketing approval for a product candidate; and
- subject to receipt of marketing approval, net revenue received from commercial sales of any of our product candidates, after milestone payments and royalty payments that we would be obligated to make.

We do not have any committed external source of funds. Our ability to raise adequate additional financing when needed, and on terms acceptable to us, will depend on many factors. These factors include investors' perceptions of the potential success of our ongoing business, including the development of our product candidates and other programs, and the potential future growth of our business. Additionally, these factors include general market conditions that also affect other companies. These factors may make raising capital difficult, and may result in us accepting terms that are unfavorable to us, especially if we are in need of financing at the particular time. The size of our company and our status as a company listed on The Nasdaq Stock Market, or Nasdaq, may also limit our ability to raise financing. For example, our ability to raise adequate financing through a public offering may be limited by market conditions and SEC rules based on our current market capitalization. Nasdaq listing rules also generally limit the number of shares we may issue in a private placement to a number less than 20% of the number of shares of our common stock outstanding immediately prior to the transaction, unless we issue

such shares at a premium, which investors may be unwilling to accept, or unless we obtain shareholder approval, which can be expensive and time-consuming and can add risk to our ability to complete the financing transaction. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate the development of our product candidates, our collaborative gene therapy sponsored research programs, or our future commercialization efforts.

We may require additional funding beyond what we currently expect due to unforeseen or other reasons. Our costs may exceed our expectations if we experience any unforeseen issue in our ongoing clinical trials, such as issues with the retention of enrolled patients or the availability of drug supply, or in our preclinical development programs, such as inability to develop formulations or if we experience issues with manufacturing, or if we further expand the scope of our clinical trials, preclinical development programs or collaborative gene therapy sponsored research programs. Our costs may also exceed our expectations for other reasons, for example, if we are required by the FDA, the EMA or regulatory authorities in other jurisdictions to perform clinical or nonclinical trials or other studies in addition to those we currently expect to conduct, if we experience issues with process development, establishing or scaling-up of manufacturing activities or activities to enable and qualify second source suppliers, or if we decide to increase preclinical and clinical research and development activities or build internal research capabilities or pursue internal research efforts. For example, we plan to begin a single Phase 3 clinical trial evaluating Zimura for GA with the expectation that data collected from such trial, together with data from our OPH2003 clinical trial, will be sufficient to seek marketing approval and we may subsequently decide to, or be required by regulatory authorities to, enroll additional patients in the Phase 3 clinical trial beyond our initial expectations or conduct additional clinical trials for Zimura in GA in order to seek or maintain regulatory approval. As a result of any of the above, we may need or may seek to obtain additional funding for our continuing operations sooner or in greater amounts than expected.

Our need for additional financing may continue even if we are able to successfully develop one or more of our product candidates. Our future commercial revenues, if any, will be derived from sales of such product candidates, which may not be available for at least several years following completion of successful product development, if at all. In addition, if approved, our product candidates may not achieve commercial success. Even if those products are successful and we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Under most, if not all, of the foregoing circumstances, we may need to obtain substantial additional financing to achieve our business objectives.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, when we can generate substantial product revenues, we may need or may seek to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our existing stockholders' ownership interests would be diluted, and the terms of these new securities may include liquidation or other preferences that adversely affect our existing stockholders' rights as common stockholders. The dilutive effect of future capital raises may be substantial, depending on the price of our common stock at the time of such capital raise, with a lower stock price translating to greater dilution for existing stockholders. Debt financing and preferred equity 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.

In addition, we have issued, and may in the future issue additional, equity securities as consideration for business development transactions, which may also dilute our existing stockholders' ownership interests. For example, under the Inception 4 Merger Agreement pursuant to which we acquired Inception 4 and our HtrA1 inhibitor program, we issued an aggregate of 5,174,727 shares of our common stock as up-front consideration to the former equityholders of Inception 4. The Inception 4 Merger Agreement also requires us to make payments to the former equityholders of Inception 4 upon the achievement of certain clinical and regulatory milestones, subject to the terms and conditions set forth in the Inception 4 Merger Agreement. Those milestone payments will be in the form of shares of our common stock, calculated based on the price of our common stock over a five-trading day period preceding the achievement of the relevant milestone, unless and until the issuance of such shares would, together with all other shares issued under the Inception 4 Merger Agreement, exceed an overall maximum limit of approximately 7.2 million shares, which is equal to 19.9% of the number of issued and outstanding shares of our common stock as of the close of business on the business day prior to the closing date of our acquisition of Inception 4, and will be payable in cash thereafter. In July 2019, we also issued 75,000 shares of our common stock to UMMS as partial upfront consideration for the in-license of our miniCEP290 program, and are obligated to issue up to 75,000 additional shares to UMMS upon the achievement of certain regulatory milestones.

In August 2018, we entered into an agreement with Cowen and Company, LLC, or Cowen, as agent, pursuant to which we may offer and sell shares of our common stock for aggregate gross sale proceeds of up to $50.0 million from time to time through Cowen under an “at-the-market” offering program, subject to the terms and conditions described in the agreement and

SEC rules and regulations. We have not yet issued and sold any shares of common stock under our "at-the-market" offering program. If we make sales under our "at-the-market" offering program, the sales could dilute our stockholders, reduce the trading price of our common stock or impede our ability to raise future capital.

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, products or product candidates or 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 grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

Our strategy of obtaining additional rights to gene therapy product candidates or technologies for the treatment of retinal diseases may not be successful.

An element of our strategy has been to expand our pipeline through in-licensing or acquiring the rights to products, product candidates or technologies that would complement our strategic goals. Since early 2018, we have completed multiple acquisition, in-license, exclusive option and sponsored research arrangements. As we have transitioned our strategy to include a focus on gene therapies, we have decided to focus our business development efforts on obtaining rights to additional gene therapy product candidates and technologies, which we will continue to evaluate on a selective basis. We may also continue to consider other alternatives, including mergers or other transactions involving our company as a whole or other collaboration transactions, including collaboration or out-license opportunities for further clinical development and potential commercialization of Zimura. Our business development efforts may fail to result in our acquiring rights to additional gene therapy product candidates or technologies, or may result in our consummating transactions with which you do not agree.

We may be unable to in-license or acquire the rights to any such gene therapy product candidates or technologies from third parties for several reasons. The success of this strategy depends partly upon our ability to identify, select and acquire or in-license promising product candidates and technologies, which is especially difficult for gene therapies. There are currently a limited number of available gene therapy product candidates or technologies for the retina and the competition for those assets is intense. Although we are planning to target opportunities where we believe third-party funding for specific programs or technologies may be available, funding may not in fact be available for any number of reasons. The process of proposing, negotiating and implementing a license or acquisition of a product candidate is lengthy and complex. For potential product candidates or technologies to which we have entered into option agreements or sponsored research agreements where we have option rights, those agreements generally do not have fixed economic or other key terms for definitive agreements, and we may not obtain favorable terms if and when we choose to exercise our option to acquire or in-license any promising product candidates or technologies.

The in-licensing and acquisition of pharmaceutical products, especially in gene therapy, is an area characterized by intense competition, and a number of companies (both more established and early stage biotechnology companies) are also pursuing strategies to in-license or acquire product candidates or technologies that we may consider attractive. More established companies may have a competitive advantage over us due to their size, cash resources and greater research, preclinical or clinical development or commercialization capabilities, while earlier stage companies may be more aggressive or have a higher risk tolerance. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to in-license or acquire the rights to the relevant product candidate or technology on terms that would allow us to make an appropriate return on our investment. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts or we may incorrectly judge the value of an acquired or in-licensed product candidate or technology.

Further, any product candidate that we acquire or in-license would most likely require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate would not be shown to be sufficiently safe and effective for approval by regulatory authorities.

If we are unable to successfully obtain rights to suitable product candidates or technologies, our business, financial condition and prospects for growth could suffer. In addition, acquisitions and in-licensing arrangements for product candidates and technologies are inherently risky, and ultimately, if we do not complete an announced acquisition or license transaction or integrate an acquired or licensed product candidate or technology successfully and in a timely manner, we may not realize the benefits of the acquisition or license to the extent anticipated and the perception of the effectiveness of our management team and our company may suffer in the marketplace. In addition, even if we are able to successfully identify, negotiate and execute one or more transactions to acquire or in-license new product candidates or technologies, our expenses and short-term costs may increase materially and adversely affect our liquidity.

In addition, acquisitions and in-licenses may entail numerous operational, financial and legal risks, including:

- exposure to known and unknown liabilities, including possible intellectual property infringement claims, violations of laws, tax liabilities and commercial disputes;
- incurrence of substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions;
- higher than expected acquisition and integration costs;
- difficulty in combining the operations and personnel of any acquired businesses with our operations and personnel;
- inability to maintain uniform standards, controls, procedures and policies;
- restructuring charges related to eliminating redundancies or disposing of assets as part of any such combination;
- large write-offs and difficulties in assessing the relative percentages of in-process research and development expense that can be immediately written off as compared to the amount that must be amortized over the appropriate life of the asset;
- increased amortization expenses or, in the event that we write-down the value of acquired assets, impairment losses;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership;
- inability to retain personnel, key customers, distributors, vendors and other business collaborators integral to an in-licensed or acquired product candidate or technology;
- potential failure of the due diligence process to identify significant problems, liabilities or other shortcomings or challenges of an acquired or licensed product candidate or technology, including problems, liabilities or other shortcomings or challenges with respect to intellectual property, product quality, revenue recognition or other accounting practices, partner disputes or issues and other legal and financial contingencies and known and unknown liabilities; and
- entry into therapeutic modalities, indications or markets in which we have no or limited direct prior development or commercial experience and where competitors in such markets have stronger market positions.

We and certain of our current and former board members and executive officers have been named as defendants in lawsuits that could result in substantial costs and divert management's attention.

We and certain of our current and former executive officers have been named as defendants in a purported consolidated putative class action lawsuit initiated in 2017 that generally alleges that we and certain of our officers violated Sections 10(b) and/or 20(a) of the Exchange Act and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning the results of our Phase 2b trial and the prospects of our Phase 3 trials for Fovista in combination with anti-VEGF agents for the treatment of wet AMD. Certain current and former members of our board of directors and current and former officers have also been named as defendants in a shareholder derivative action initiated in August 2018, which generally alleges that the defendants breached their fiduciary duties to our company by failing to oversee our business during the period of the Phase 2b and Phase 3 clinical trials of Fovista. These complaints seek equitable and/or injunctive relief, unspecified damages, attorneys' fees, and other costs. In September 2019, the court issued an order dismissing some, but not all, of the allegations in the class action lawsuit and denied our motion to dismiss the shareholder derivative action. We and the defendants continue to deny any and all allegations of wrongdoing and intend to vigorously defend against these lawsuits. We are unable, however, to predict the outcome of these matters at this time. Moreover, any conclusion of these matters in a manner adverse to us and for which we incur substantial costs or damages not covered by our directors' and officers' liability insurance would have a material adverse effect on our financial condition and business. In addition, the litigation could adversely impact our reputation and divert management and our board of directors' attention and resources from other priorities, including the execution of our business plan and strategies that are important to our ability to grow our business, any of which could have a material adverse effect on our business. Additional lawsuits may be filed.

The comprehensive tax reform bill passed in December 2017 could adversely affect our business and financial condition.

In December 2017, United States President Donald J. Trump signed into law new legislation that significantly revised the Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat

rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modification or repeal of many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. The United States Department of Treasury and the Internal Revenue Service are continuing to issue new guidance and interpretations of various provisions of the new tax law. In addition, various states have responded in different ways to the new federal tax law. The impact of this new tax law on holders of our common stock is also uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

Risks Related to Product Development and Commercialization

Companies in our industry face a wide range of challenging activities, each of which entails separate, and in many cases substantial, risk.

The long-term success of our company, and our ability to become profitable as a biopharmaceutical company, will require us to be successful in a range of challenging activities, including:

- designing, conducting and successfully completing preclinical research and development activities, including preclinical efficacy and IND-enabling studies, for our product candidates or product candidates we are interested in in-licensing or acquiring, including those we may evaluate as part of our collaborative gene therapy sponsored research programs;
- making arrangements with third-party manufacturers and providers of starting materials for our product candidates, and having those manufacturers successfully develop manufacturing processes for drug substance and drug product and provide adequate amounts of drug product for preclinical and clinical activities in accordance with our expectations and regulatory requirements;
- designing, conducting and completing clinical trials for our product candidates;
- obtaining favorable results from required clinical trials, including for each ophthalmic product candidate, favorable results from two adequate and well-controlled pivotal clinical trials in the relevant indication;
- applying for and receiving marketing approvals from applicable regulatory authorities for the marketing and sale of our product candidates;
- making arrangements with third-party manufacturers for scale-up and commercial manufacturing, receiving regulatory approval of our manufacturing processes and our third-party manufacturers' facilities and ensuring adequate supply of drug product and starting materials used for the manufacture of drug product;
- establishing sales, marketing and distribution capabilities, either internally or through collaborations or other arrangements, to effectively market and sell our product candidates, if and when approved;
- achieving acceptance of the product candidate, if and when approved, by patients, the medical community and third-party payors;
- if our product candidates are approved, obtaining from governmental and third-party payors adequate coverage and reimbursement for our product candidates and, to the extent applicable, associated injection procedures conducted by treating physicians;
- effectively competing with other therapies, including the existing standard of care, and other forms of drug delivery;
- maintaining a continued acceptable safety profile of the product candidate during development and following approval;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity, including under the Orphan Drug Act and the Hatch-Waxman Amendments to the Federal Food, Drug and Cosmetic Act, or FDCA, if we choose to seek such protections for any of our product candidates;
- protecting and enforcing our rights in our intellectual property portfolio; and

- complying with all applicable regulatory requirements, including FDA Good Laboratory Practices, or GLP, FDA Good Clinical Practices, or GCP, current Good Manufacturing Practices, or cGMP, and standards, rules and regulations governing promotional and other marketing activities.

Each of these activities has associated risks, many of which are detailed below and throughout this "Risk Factors" section. We may never succeed in these activities and, even if we do, may never generate revenues from product sales that are significant enough to achieve commercial success and profitability. Our failure to be commercially successful and profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or continue our operations. A decrease in the value of our company would also cause our stockholders to lose all or part of their investment.

Drug development is a highly uncertain undertaking. Our research and development efforts may not be successful or may be delayed for any number of reasons, in which case potential clinical development, marketing approval or commercialization of our product candidates could be prevented or delayed.

Before obtaining approval from regulatory authorities for the sale of any product candidate, we must conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Prior to initiating clinical trials, a sponsor must complete extensive preclinical testing of a product candidate, including, in most cases, preclinical efficacy experiments as well as IND-enabling toxicology studies. Drug research, including the gene therapy research we are sponsoring with UMMS, may never yield a product candidate for preclinical or clinical development. Early stage and later stage research experiments and preclinical studies may fail at any point for any number of reasons, and even if completed, may be time-consuming and expensive. As a result of these risks, a potentially promising product candidate may never be tested in humans.

Once it commences, clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. For example, our pivotal Phase 3 Fovista program for the treatment of wet AMD failed to produce positive safety and efficacy data that support the use of Fovista in wet AMD, despite the results from preclinical testing and earlier clinical trials of Fovista, including a large Phase 2b trial with statistically significant efficacy signal. Furthermore, our Phase 2a OPH2007 safety trial of Zimura in combination with the anti-VEGF agent Lucentis in wet AMD did not replicate the results of our Phase 1/2a OPH2000 trial. Additionally, although the results we have received to date from our OPH2003 clinical trial confirm that Zimura met the prespecified primary endpoint in reducing the mean rate of GA growth in patients with dry AMD with statistical significance across both the Zimura 2mg and Zimura 4 mg treatment groups when compared to the corresponding sham control groups, these results may be undermined by inconsistent data obtained from the final results from this clinical trial or may not be replicated in any future clinical trials evaluating Zimura for GA. Preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

We may experience numerous unforeseen events during drug development that could delay or prevent our ability to receive marketing approval or commercialize our product candidates. These risks include, but are not limited to, the following:

- we may not be able to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation of clinical trials for any preclinical product candidates that we are developing or may wish to in-license or acquire;

- we or our contract manufacturers may be unable to develop a viable manufacturing process for any product candidates that we are developing;

- the supply or quality of our product candidates or other materials necessary to conduct preclinical development and clinical trials of our product candidates may be insufficient or inadequate or we may face delays in the manufacture and supply of our product candidates for any number of reasons, including as a result of interruptions in our supply chain, including in relation to the procurement of starting materials, such as plasmids used for the manufacture of our gene therapy product candidates, and the packaging, distribution, storage and import/export of materials and products;

- we or our contract research organizations may be unable to complete necessary analytical development for and testing of our product candidates, including assays for assessing the potency of our gene therapy product candidates;

- regulators or institutional review boards may not agree with our clinical trial designs, including our selection of endpoints, or may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;

- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective contract research organizations or clinical trial sites, especially in cases where we are working with contract research organizations or clinical trial sites we have not worked with previously;

- our contract research organizations, clinical trial sites, contract manufacturers, providers of starting materials and packagers and analytical testing service providers may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;

- we, through our clinical trial sites, may not be able to locate and enroll a sufficient number of eligible patients to participate in our clinical trials as required by the FDA or similar regulatory authorities outside the United States, especially in our clinical trials for orphan or other rare diseases;

- we may decide, or regulators or institutional review boards may require us, to suspend or terminate clinical trials for various reasons, including noncompliance with regulatory requirements, including GCPs, or a finding that the participants are being exposed to unacceptable health risks;

- as there are no therapies approved for many of the indications we are seeking to treat, including GA, in either the United States or the European Union, the regulatory pathway for product candidates in those indications, including the selection of the primary efficacy endpoint for a pivotal clinical trial, is highly uncertain;

- there may be changes in regulatory requirements and guidance or we may have changes in trial design that require amending or submitting new clinical trial protocols;

- there may be changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;

- we may decide, or regulators may require us, to conduct additional clinical trials beyond those we currently contemplate or to abandon product development programs;

- the number of patients required for clinical trials of our product candidates to demonstrate statistically significant results 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. These risks may be heightened for clinical trials in orphan diseases, for which the natural history of the disease is less understood, making it more difficult to predict the drug effect required to adequately demonstrate efficacy, and because there are fewer affected individuals available to participate in clinical trials; and

- the cost of clinical trials of our product candidates may be greater than we anticipate.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;

- not obtain marketing approval at all;

- obtain approval for indications or patient populations that are not as broad as intended or desired;

- obtain approval with labeling that includes significant use limitations, distribution restrictions or safety warnings, including boxed warnings;

- be subject to additional post-marketing testing requirements; or

- have the product removed from the market after obtaining marketing approval.

Despite our ongoing efforts, we may not complete any of our ongoing or planned development activities for our product candidates. The timing of the completion of, and the availability of results from, development activities, especially clinical trials, is difficult to predict. For clinical trials in particular, we do not know whether they will begin as planned, will need to be restructured or will be completed on schedule, or at all. Furthermore, our development plans may change based on feedback we may receive from regulatory authorities throughout the development process. For example, our expectations regarding the remaining clinical requirements to demonstrate the safety and efficacy of Zimura for the treatment of GA

secondary to dry AMD in a manner sufficient to support an application for regulatory approval to the FDA and EMA are based on our review of initial, top-line data from the OPH2003 trial as well as preliminary, informal discussions with the FDA. We may or may not have further interactions with the FDA or other regulatory authorities prior to commencing our Phase 3 clinical trial. Our expectations regarding the minimum clinical requirements to demonstrate the safety and efficacy of Zimura for GA could be incorrect or may change as we continue to review and analyze the OPH2003 trial 12-month clinical data set, as 18-month clinical data from the OPH2003 trial becomes available, and as new regulatory or third party information, including third-party clinical data or information from prospective collaborators or licensees, becomes available. If we experience delays in manufacturing, testing or marketing approvals, our product development costs would increase. Significant product development delays also could allow our competitors to bring products to market before we do, impair our ability to successfully commercialize our product candidates, including by shortening any periods during which we may have the exclusive right to commercialize our product candidates, and may otherwise harm our business and results of operations.

Our development of Zimura is based on a novel mechanism of action that is unproven and poses a number of scientific and other risks, and we may not be successful in developing Zimura in the indications we are pursuing.

We are targeting GA, an advanced form of dry AMD, and STGD1 with Zimura. The causes of AMD are not completely understood. In addition to advanced age, there are environmental and genetic risk factors that contribute to the development of AMD including ocular pigmentation, dietary factors, a positive family history for AMD, high blood pressure and smoking. Although we believe there is a scientific rationale for pursuing the development of inhibitors for selective molecular targets, including complement C5, as potential pharmaceutical treatments for AMD, and that the initial, top-line data from our OPH2003 trial of Zimura in GA support our view, this approach may not prove successful for treating AMD in a clinically meaningful way. Similarly, although there is non-clinical scientific literature supporting the potential use of inhibitors of the complement system for the treatment of STGD1, this approach may not prove clinically successful as well.

Zimura is designed to inhibit complement C5. There are no FDA or EMA approved products that utilize C5 inhibition as a mechanism of action to treat GA or STGD1. There have been other investigational products using complement inhibition as a mechanism of action for the treatment of GA, including inhibition of C5, that proved to be unsuccessful, even in later-stage clinical trials. Even though our OPH2003 trial of Zimura in GA met its prespecified primary endpoint, this mechanism of action may not prove safe and effective for the treatment of GA, STGD1 or any other indication for which we may develop Zimura.

The results we observed from the OPH2003 trial may not be supported by the final results of this trial or may not be fully replicated in subsequent clinical trials. A future clinical trial evaluating Zimura for GA may use a different design, which may subject the outcome of that trial to regulatory uncertainty and other known and unknown factors.

The results we observed from our OPH2003 trial of Zimura in GA may not be supported by the final results of this trial or may not be fully replicated in subsequent clinical trials evaluating Zimura for GA. In accordance with the clinical trial protocol, we will continue to treat and follow patients through the 18-month time point to collect additional safety and efficacy data, including mean GA area and mean change in BCVA and LL BCVA by treatment group. Although we do not plan to perform any prespecified statistical analysis with respect to these data, these data may indicate an unexpected or unknown safety issue, including increased incidence of CNV, or may indicate the loss of efficacy for Zimura during the period between month 12 and month 18. After month 18, we expect to receive and analyze individual patient data on an unmasked basis following completion of the trial by all patients. We expect that the unmasked individual patient data will provide us a better understanding of the results and the variables affecting the results, although it may indicate that our initial conclusions were not well founded due to inconsistencies, data entry errors or because of unknown variables or patient sub-groups that could potentially be driving the results in one or more treatment groups. At this time, we cannot verify that GA images have been measured accurately or review the images for consistency with our hypotheses and the conclusions from this trial.

We intend to explore all options for the future development and potential commercialization of Zimura. We are in the process of determining several key elements of the design of our Phase 3 clinical trial of Zimura in GA, such as number of patients, the dosage level or levels, the treatment arms, the frequency of dosing and other factors. Several Phase 3 clinical trials for ophthalmic product candidates that have been, or are currently being, conducted by other sponsors include multiple treatment arms, either different doses or treatment regimens, in addition to a control arm. The FDA has expressed that including multiple doses or treatment regimens within a single trial helps mitigate the risk of bias in the trial. We believe that the anatomical measure used as the primary efficacy endpoint in our OPH2003 trial, the mean rate of change in GA growth, as evaluated by an independent, masked reading center, is not subject to bias. We may therefore proceed with only one treatment arm in our pivotal Phase 3 clinical trial of Zimura in GA, especially given the treatment burden associated with the Zimura 4mg dose evaluated in our OPH2003 trial. However, the FDA, EMA or other regulatory authorities may disagree with our view. In addition, the dose that we choose to pursue, may not prove to be efficacious in our pivotal Phase 3 clinical trial of Zimura in GA. Alternatively, if, in addition to including a Zimura 2mg treatment group, we include a Zimura 4 mg treatment group in an attempt to satisfy regulatory expectations and as we currently have for the OPH2003 trial, patients may find the treatment regimen in either group to be too burdensome and may withdraw from our trial in greater numbers than we expect, making it

more difficult to demonstrate a clinically relevant benefit with statistical significance and in a robust fashion. Another possibility we may consider is to evaluate dosing levels or regimens that we have not previously studied, such as dosing less frequently than monthly throughout the clinical trial, including during the first 12 months of the trial. We cannot predict whether dosing levels or treatment regimens we have not previously studied will prove effective in treating GA. Moreover, the previously unstudied does level or treatment regimen may demonstrate efficacy in our Phase 3 clinical trial, while a previously studied monthly dose may not. These findings would be inconsistent with our findings in the OPH2003 trial to date, and if this were to occur, we would not have data from an independent, well-controlled clinical trial available to seek regulatory approval of the alternative dose or treatment regimen. Regardless of the design that we choose, the FDA, EMA or other regulatory authorities may ultimately not accept the data from our Phase 3 clinical trial of Zimura in GA, together with data from the OPH2003 trial, even if we believe the data from these trials demonstrate a clinically relevant benefit with statistical significance and in a robust fashion.

Our intended regulatory pathway for generating sufficient safety and efficacy data to submit an NDA and potentially obtain marketing approval for Zimura for GA is subject to a number of assumptions, including that we can rely on the results from our OPH2003 trial as one of two well-controlled, pivotal trials typically required by the FDA. The FDA, EMA and other regulatory authorities may not accept the results of the OPH2003 as a pivotal clinical trial, or may not agree with our selection of primary endpoint or the statistical analysis we performed. We may decide to or be required to enroll additional patients, collect additional safety data or conduct additional trials.

Based on the results we have received to date from our OPH2003 international, randomized, double masked, sham controlled, multi-center clinical trial, additional statistical analysis we have performed and preliminary, informal discussions we have had with the FDA, we believe that the efficacy results from this trial could potentially satisfy the FDA's requirements as one of the two pivotal clinical trials typically required for marketing approval. This belief is based on many assumptions, including that a reduction in mean rate of GA growth is a primary endpoint of clinical relevance, in the absence of a demonstrated reduction in the loss of vision, and that data from the OPH2003 trial is robust. The FDA, the EMA or other regulatory authorities may not agree with our view that the observed reduction in the rate of GA growth is clinically relevant or meaningful, or may require us to correlate this reduction in rate of GA growth with another outcome more directly associated with visual function, such as reduced rate in the loss of visual acuity. The FDA, the EMA or other regulatory authorities may disagree with our conclusion regarding the robustness of the data from this trial based on our sensitivity analyses or may conduct their own sensitivity analyses yielding different results. We likely will not have an opportunity to obtain definitive confirmation from the FDA, EMA or other regulatory authorities regarding the robustness of the data from our clinical trials, including the OPH2003 trial of Zimura in GA, until such time as we submit an application for regulatory approval and receive a response from the applicable authority. If the OPH2003 trial results are not considered robust, in order to seek marketing approval we may need to conduct, in addition to the Phase 3 clinical trial for which we are commencing site selection and planning activities, one or more additional, well-controlled clinical trials that meets the applicable regulatory requirements in order to obtain sufficiently robust data to support regulatory approval.

The FDA, EMA or other regulatory authorities may not agree with the methodologies we used to perform the statistical analysis of the OPH2003 trial results. In particular, they may not agree with how we performed the comparisons of patients receiving Zimura 2mg with patients in the sham groups, as the comparisons draw upon patients that were enrolled into two different parts of the trial, using different randomization ratios and different vision criteria. In addition, they may not agree with the validity of our MRM analysis, which imputes the values of missing data based on observed data. Moreover, the FDA, EMA or other regulatory authorities may disagree with our inclusion in our efficacy analysis of patients who do not strictly meet all eligibility criteria, or whose treatment or assessments in the clinical trial deviated from the clinical trial protocol on one or more occasions. The FDA, EMA or other regulatory authorities may take issue with the degree of data that are missing from our OPH2003 clinical data set, or with the rate at which patients withdrew from the trial.

Although we believe that our OPH2003 trial was well-controlled, with appropriate eligibility criteria and appropriate stratification for baseline characteristics, the FDA, EMA or other regulatory authorities may not agree with the methodologies we used to determine patient eligibility and randomize patients to the various treatment groups and therefore may not agree that the comparisons we have made for mean rate of GA growth are statistically valid. The FDA, EMA or other regulatory authorities may take issue with the number of modifications we introduced to the OPH2003 trial following its commencement, which they may view as introducing additional uncontrolled variables, invalidating the comparisons across groups. In particular, the FDA, EMA or other regulatory authorities may view the change in enrollment criteria applied in the various modifications as changing the nature of the patients enrolled, thus rendering the results of the trial as uninterpretable, or may disagree with our decision to remove patients who develop CNV in their study eye from future treatments and assessments as inappropriate, concluding that it may have resulted in unmitigated or uncontrolled bias in the efficacy results from the trial.

Based on preliminary, informal discussions with the FDA, we believe we need to conduct an additional clinical trial consisting of at least 300 patients, with primary endpoints at 12 months or later, and with safety data collected for at least 24

months. For the safety data, we believe we can rely on safety data from our OPH2005 trial evaluating Zimura for STGD1 and we can finish collecting safety data after submitting for marketing approval. These assumptions about the additional clinical trial required for submission of an application for regulatory approval of Zimura in GA and the need to collect safety data are subject to review by the FDA, EMA and other regulatory authorities, who may require us to enroll additional patients, collect additional safety data, conduct additional trials or take other actions, which may increase the costs of our Zimura clinical programs and delay our expected timelines.

Furthermore, our previous and ongoing Zimura clinical trials have evaluated Zimura dosing levels and regimens that we have studied only in cohorts consisting of a small number of patients. This approach may increase the risk that patients in our ongoing trials experience adverse events and/or serious adverse events (either ocular, systemic or both) that we have not observed or at rates that we have not observed in prior trials. Although we did not observe adverse events or serious adverse events attributable to the drug product in our OPH2003 trial, previously unobserved adverse events and/or serious adverse events may manifest in the remaining portion of our OPH2003 trial, in our OPH2005 trial or in any subsequent clinical trials we or a potential licensee or collaborator may undertake for Zimura. When we follow patients for a longer period of time or collect safety data from a greater number of patients, we may obtain safety data that we have not previously observed. For a further discussion of the safety risks in our trials, see the risk factor herein entitled "*If serious adverse or unacceptable side effects are identified during the development of our product candidates, we may need to abandon or limit our development of such product candidates.*"

Our ongoing and any future clinical trials for Zimura that we or a potential future licensee or collaborator may undertake may fail to demonstrate sufficient safety or efficacy to justify further development or to ultimately seek or obtain marketing approval. Any negative results from our ongoing or any future clinical trials for Zimura could adversely affect our business and the value of your investment in our company.

We have no human clinical data regarding the safety and efficacy of Zimura as a treatment of STGD1. The drop-out rate may reduce the number of patients from whom we can collect and analyze data from our OPH2005 trial.

We have no human clinical data regarding the safety and efficacy of Zimura as a treatment for STGD1. In addition, although we initially determined the size of the OPH2005 trial in STGD1 based on the number of patients with STGD1 that we believed could potentially be enrolled within a reasonable period of time, we decided to cease patient enrollment during the first quarter of 2019 in light of the 18-month endpoint and our goal of providing initial top-line data from this trial by the end of 2020. As STGD1 is an orphan indication, to our knowledge there is only very limited natural history data currently available regarding the variability for our planned primary efficacy endpoint in the STGD1 patient population we enrolled in this trial. Moreover, because Stargardt disease, like GA, is a degenerative disease, and in many cases, the rate of degeneration is slow, and because we are seeking to slow the progression of degeneration with Zimura, and not necessarily to reverse prior degeneration or restore visual function, patients participating in our OPH2005 trial, who may be younger and may experience vision loss that is more subtle than patients with GA or AMD, may not perceive a benefit from continuing to participate and therefore may drop out of this trial. Although we and the investigators and their staff take efforts to encourage continued patient participation, the drop-out rate may exceed our expectations. A higher than expected drop-out rate would reduce the number of patients from whom data is available for analyzing the primary endpoint for this trial. Given the information above, our OPH2005 trial could be underpowered to demonstrate a potential clinical benefit for Zimura in STGD1 with statistical significance.

Gene therapy is an emerging field of drug development that poses many scientific and other risks. We have only limited prior experience in gene therapy research and manufacturing and no prior experience in gene therapy clinical development. Our lack of experience may limit our ability to be successful or may delay our development efforts.

Gene therapy is an emerging field of drug development with only two gene replacement therapies having received FDA approval to date. Our gene therapy research and development programs, which we decided to undertake based on a review of a limited set of preclinical data, are still at an early stage. Even with promising preclinical data, there remains several areas of drug development risk, including translational science, manufacturing materials and processes, safety concerns, regulatory pathway and clinical trial design and execution, which pose particular uncertainty for our programs given the relatively limited development history of, and our limited prior experience with, gene therapies. Furthermore, the medical community's understanding of the genetic causes of many diseases continues to evolve and further research may change the medical community's views on what therapies and approaches are most effective for addressing certain diseases.

For example, while there are more than 200 known mutations to the *BEST1* gene, the different types of mutations and their association with various *BEST1*-related IRDs are still not well-understood. Our product candidate for these diseases, IC-200, may only be effective in treating retinal diseases associated with certain mutations in the *BEST1* gene and not other mutations. Additionally, we decided to in-license and pursue the development of IC-200 based on results observed in an autosomal recessive canine disease model. A majority of humans with *BEST1*-related IRDs, however, have the autosomal dominant form of the disease, commonly referred to as Best disease. If we choose to develop IC-200 for this patient population, using a construct previously studied in an autosomal recessive canine disease model, this approach may ultimately prove ineffective.

For our miniCEP290 program and other minigene programs, we are sponsoring research using a novel approach that is largely untested and presents various scientific and regulatory risks. To date, all the data generated for our miniCEP290 program are in a newborn mouse model for LCA10, and we do not know whether the effect we observed with these minigenes in mice will be replicated in other animals or humans. Furthermore, minigenes result in the expression of a protein that differs from the naturally occurring protein. The protein expressed by the minigene may have physiological effects, including toxic effects, that are not yet known. Because of the novelty of minigenes, the medical community's and regulators' receptiveness to this approach remains unknown. Our sponsored research may not fully elucidate all of the physiological risks associated with a particular minigene and the associated expressed protein. For these and other reasons, promising minigene candidates that emerge from our sponsored research programs with UMMS may not succeed in later stage preclinical and clinical development.

We have particularly focused on adeno-associated virus, or AAV, gene therapy, as AAV vectors are relatively specific to retinal cells and their safety profile in humans is relatively well-documented as compared to other delivery vehicles and gene therapy technologies currently in development. However, AAV has a number of drawbacks, including its small packaging capacity: an AAV vector can hold only up to approximately 4,700 base pairs of DNA, whereas the genes that are associated with a number of diseases, such as LCA10, Stargardt disease and Usher 2A, exceed that size. Although AAV is the most commonly used vector in ocular gene therapy today, it may prove to pose safety risks that we are not aware of and other vector forms, such as retroviral or lentiviral and non-viral based vectors, or gene editing approaches, may prove to be safer and more effective.

Although we believe gene therapy is a promising area for retinal drug development, our gene therapy research and development experience is limited to only a few personnel hired to supervise our outside service providers. In pursuing this new technology, we have begun to establish our own gene therapy technical capabilities, but we will need to continue to build those capabilities by either hiring internally or seeking assistance from outside service providers. We believe that gene therapy is an area of significant investment by biotechnology and pharmaceutical companies and that there may be a scarcity of talent available to us in these areas. If we are not able to expand our gene therapy capabilities, we may not be able to develop in the way we intend or desire, IC-100, IC-200 or any promising product candidates that emerge from our miniCEP290 program or our other collaborative gene therapy sponsored research programs, which would limit our prospects for future growth.

For a further discussion of the risks associated with the manufacturing of gene therapy products, see the risk factor herein entitled "*The manufacture of gene therapy products is complex with a number of scientific and technical risks, some of which are common to the manufacture of drugs and biologics and others are unique to the manufacture of gene therapies. We have limited experience with gene therapy manufacturing and are dependent on our third-party contract manufacturers and sole source suppliers*".

Our development of our HtrA1 inhibitor program is also based on a novel mechanism of action that is unproven and poses a number of scientific and other risks. We may not be able to successfully formulate a product candidate from our HtrA1 inhibitors or identify a product candidate with a viable manufacturing process.

Our HtrA1 inhibitor program is in preclinical development. There are no FDA or EMA approved products that utilize HtrA1 inhibition as a mechanism of action for treating ophthalmic diseases, including GA and other age-related retinal diseases for which we may develop our HtrA1 inhibitor program, and this mechanism of action may not prove safe and effective for these diseases. We made the decision to acquire this program based on our interpretation of the scientific literature and rationale for this potential target that suggest an association between HtrA1 and the risk for AMD, as well as a limited set of preclinical data generated by Inception 4 prior to the acquisition. We note, however, the *HtrA1* gene is in the same region of the 10q26 chromosome as the *age-related maculopathy susceptibility 2*, or *ARMS2*, gene. The *ARMS2* and *HtrA1* genes are linked, and variants in, or expression of, the *ARMS2* gene may also be associated with the risk for AMD. The risk for AMD associated with *ARMS2* may ultimately prove to be greater than the risk associated with *HtrA1*. In addition, even though genetic and histologic findings correlate HtrA1 with AMD, the development and progression of AMD may not be affected by HtrA1. Our assumption that targeting inhibition of HtrA1 as a method of treating AMD may be incorrect, which would likely adversely affect the value of our HtrA1 inhibitor program and its continued development.

Before we can commence IND-enabling studies for our HtrA1 inhibitor program, we need to conduct process development and formulation development with our lead compounds in this program to determine whether we can identify a viable manufacturing process for and formulate a product candidate for intravitreal administration that is safe to advance into preclinical studies and, depending on the outcome of such studies, into clinical trials. For example, as part of formulation development, we need to determine which inactive formulation components should be used in the preparation of the product candidate, and derive a preparation that includes an adequate amount of drug substance with the necessary inactive ingredients to achieve the desired safety profile for intravitreal injection into the eye while providing for sufficient pharmacological activity. Process development and formulation development are inherently uncertain, and it is possible we may not be able to identify a viable manufacturing process for or formulate any of our lead compounds into a preparation that is safe to advance into preclinical studies or clinical trials in the eye or that provides sufficient pharmacological activity, which would hinder our ability to pursue development of this program. Manufacturing, including process development, and formulation development can be time-consuming and our anticipated timelines for the development of this program may be delayed.

If serious adverse or unacceptable side effects are identified during the development of our product candidates, we may need to abandon or limit our development of such product candidates.

If any of our product candidates are associated with serious adverse events or undesirable side effects in preclinical studies or clinical trials or have characteristics that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause side effects that prevented further development of the compound.

To date, we currently have safety data from a total of 113 patients receiving monthly treatments of either Zimura 2mg or Zimura 4mg for a minimum of 12 months in the OPH2003 trial. In our completed clinical trials for Zimura, we have observed only a single adverse event, mild subcapsular cataract, from our OPH2000 trial, assessed to be drug-related by participating investigators. We have no data regarding the safety, tolerability or efficacy of Zimura administered for the treatment of STGD1. We have no human data regarding IC-100, IC-200 or any of our HtrA1 inhibitors.

Our clinical trials for Zimura involve dosing regimens that we have not studied extensively, which may increase the risk that patients in these trials experience adverse events and/or serious adverse events (either ocular, systemic or both) that we have not observed or at rates that we have not observed in prior trials. For example, although the reduced rate of growth in GA we observed in the OPH2003 trial has not been associated with disproportionate loss of vision in the treated groups as compared to the sham control groups over the first 12 months of the trial, we may observe increased loss of vision in the Zimura treatment groups, as compared to the corresponding sham control arms, during the period between month 12 and month 18 in the trial or in our Phase 3 clinical trial of Zimura in GA. In addition, although we view the rate of CNV incidence in the Zimura treatment groups, as compared to the corresponding sham control groups, as acceptable and within the range observed in other clinical trials of complement inhibitors in development for GA, the FDA, EMA, other regulatory authorities, treating physicians or patients may not agree, concluding that Zimura may increase the risk of patients developing CNV to an unacceptable degree. Moreover, our clinical trials for Zimura involve multiple intravitreal injections over an extended period of time and, as such, may involve risks regarding multiple and chronic intravitreal injections. For these reasons, there may be, among others, an increase in the rates of intraocular infections, or endophthalmitis, intraocular pressure, glaucoma, retinal tears, cataracts, retinal detachment, intraocular inflammation, retinal and/or choroidal circulation compromise, or hospitalizations in patients who receive Zimura. For our OPH2003 trial, once all patients reach the 18 month time point, we expect that we will receive complete safety data, including unmasked data covering the period between month 12 and month 18. An unforeseen or unexpected safety issue, or any safety finding that is inconsistent with our prior experience with Zimura, including during the first 12 months of the OPH2003 trial, from any of our clinical trials for Zimura may impact our ability to continue to develop Zimura or the long-term viability of Zimura as a potential treatment for GA, STGD1 or any other indication for which we may seek to develop Zimura.

As HtrA1 inhibition is a novel treatment approach for treating ocular disease, this treatment modality may present potentially unknown safety risks when tested in clinical trials that could not have been anticipated based on preclinical toxicology studies. In addition, if we are successful in formulating an HtrA1 product candidate, we intend to administer the product candidate by intravitreal injection, which poses the same safety risks outlined above with respect to intravitreal injections of Zimura.

In addition, there are several known safety risks specific to gene therapy, including inflammation resulting from a patient's immune response to the administration of viral vectors and the potential for toxicity as a result of chronic exposure to the expressed protein. Managing a host body's immune response to introduced viral vectors has been and remains a challenge for gene therapies. For AAV gene therapy, "vector shedding," or the dispersal of AAV vectors away from the target tissue to other parts of the body, which can trigger a more serious and extensive immune response, is a known safety issue. Although subretinal injection, which is the method often used to administer ocular gene therapies, helps to control vector shedding

beyond the eye, subretinal injection is a surgical procedure that requires significant skill and training for the administering surgeon and involves its own risks separate from the gene therapy vectors, including the risk of retinal detachment. The margin for error with subretinal injections is extremely low and there are a limited number of retinal surgeons with experience in performing subretinal injections in the eye. In order to generate useful clinical data for gene therapy clinical trials, a retinal surgeon must repeat the same subretinal injection process multiple times and with consistency. In addition, in order to avoid accelerating damage to a subject's retina, subretinal injection for RHO-adRP patients in particular must be conducted under extremely low light levels using infrared technology, further complicating the surgical procedure. In the event that we progress into clinical development with IC-100, IC-200 or any other gene therapy product candidate we may in-license or acquire, we may experience delays or other challenges for our gene therapy development programs as a result of safety issues.

In addition to the currently known safety risks, there may be unknown risks to human health from gene therapies. Because gene therapy involves the introduction of concentrated quantities of AAV, as well as the introduction of persistent foreign genetic material into the human body, any safety risks may not manifest until much later, if at all. Gene therapies have only recently been used in the treatment of human diseases and the scientific and medical understandings of safety or other risks to humans continue to evolve. The safety profile of minigenes and their associated proteins in humans remains largely unknown. If gene therapies prove to be unsafe for humans, we likely will need to curtail or eliminate our gene therapy development programs or gene therapy products in development or commercialization, if any.

We do not have any internal manufacturing capabilities and use third parties to manufacture our product candidates on a contract or purchase order basis. Manufacturing issues, including technical or quality issues or issues with scaling up and building our capabilities for later-stage clinical manufacturing or for commercial manufacturing, may arise that could cause delays in our development programs or increase costs. We may experience delays in regulatory approval of our product candidates if we or our contract manufacturers do not satisfy applicable manufacturing regulatory requirements.

We do not have internal manufacturing facilities and use or plan to use outside contract manufacturers to manufacture Zimura, IC-100, IC-200, our HtrA1 inhibitors and any other product candidates that we may acquire or in-license. We have a limited number of personnel hired to supervise these outside vendors. Manufacturing for these product candidates could be complicated or present novel technical challenges. Problems with the manufacturing process, even minor deviations from the established process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims or insufficient inventory. We may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

In addition, in order to manufacture and supply any of our product candidates for later-stage clinical trials or on a commercial scale in the future, we will need to increase our manufacturing personnel and bolster our quality control and quality assurance capabilities. We may encounter problems hiring and retaining scientific, manufacturing and quality assurance and control personnel needed to oversee our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements. As we or any manufacturer we engage scales up manufacturing of any product candidate, we may encounter unexpected issues relating to the manufacturing processes or the quality, purity or stability of the product, and we may be required to refine or alter our manufacturing processes to address these issues. Resolving these issues could result in significant delays and may result in significantly increased costs. If we underestimate the demand for an approved product, given the long lead times required to manufacture or obtain regulatory approvals for our products, we could potentially face commercial drug product supply shortages. If we experience significant delays or other obstacles in producing any approved product at commercial scale, our ability to market and sell any approved products may be adversely affected and our business could suffer.

The manufacturing processes and the facilities of our third-party manufacturers are subject to inspection and approval by the FDA, referred to as a pre-approval inspection, before we can commence the commercial sale of any approved product candidate, and thereafter on an ongoing basis. Our third-party drug substance manufacturer for Zimura has undergone only two pre-approval inspections by the FDA, and has not yet gone through a pre-approval inspection for Zimura. Failure by our third-party manufacturers to pass such inspections and otherwise satisfactorily complete the FDA approval regimen with respect to our product candidates may result in delays in the approval of our applications for marketing approval, as well as regulatory actions such as the issuance of FDA Form 483 notices of observations, warning letters or injunctions or the loss of operating licenses. If any of our third-party manufacturers are found to have delayed, denied, limited or refused a drug inspection, our drug substance or drug product could be deemed adulterated. Based on the severity of the regulatory action, our clinical or commercial supply of drug substance or drug product could be interrupted or limited, which could have a material adverse effect on our business.

Any problems in our manufacturing process or our third-party contract manufacturers' facilities could make us a less attractive collaborator for potential collaborators, including larger pharmaceutical companies and academic research

institutions, which could limit our access to additional attractive development programs. Problems in our manufacturing process or facilities also could restrict our ability to meet market demand for our products.

For a further discussion of the risks associated with our reliance on third-party manufacturers, see the risk factor herein entitled, "*We contract with third parties for the manufacture of and for providing starting materials for our product candidates for preclinical development activities and clinical trials and expect to continue to do so in the future. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products, which could delay, prevent or impair our development or commercialization efforts.*"

Our experience manufacturing Zimura is limited. We and our third-party contract manufacturers have not scaled up or validated the manufacturing process for Zimura for later-stage clinical or commercial manufacturing. We are only in the early stages of establishing manufacturing capabilities for our HtrA1 inhibitor program.

We currently use a single third-party manufacturer, Agilent Technologies, to supply us with the chemically synthesized drug substance for Zimura and a different, single third-party manufacturer, Ajinomoto Bio-Pharma Services, to provide fill/finish services for Zimura. In order to obtain and maintain regulatory approval for Zimura, our third-party manufacturers will be required to consistently produce the drug substance used in Zimura in commercial quantities and of specified quality and to execute fill/finish services on a repeated basis and document their ability to do so. If the third-party manufacturers are unable to satisfy this requirement, our business would be materially and adversely affected. We have not manufactured clinical supplies of Zimura since early 2017 and we may need to perform additional work beyond what we currently plan to reestablish our manufacturing and analytical capabilities. To date, we have not yet scaled up the manufacturing process for Zimura beyond the scale used for developmental clinical batches, nor have we validated the manufacturing process. Even if we successfully complete any required clinical trials for Zimura and obtain sufficient and favorable safety and efficacy data, we will need to scale up and validate our manufacturing process before we can obtain marketing approval for Zimura, and any such scale-up and validation activities may be costly, time-consuming and uncertain in outcome.

Some of the standards of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, which establishes basic guidelines and standards for drug development in the United States, the European Union, Japan and certain other countries, do not apply to oligonucleotides, including aptamers. As a result, there are limited established generally accepted manufacturing or quality standards for the production of Zimura. The lack of uniform manufacturing and quality standards among regulatory agencies may delay regulatory approval of Zimura.

For our HtrA1 inhibitor program, we have engaged a CDMO to produce small quantities of the active pharmaceutical ingredient, or API, of our HtrA1 inhibitors for preclinical development purposes. We expect to engage a CDMO to conduct process development, scale-up and GMP manufacture of the API of our HtrA1 inhibitors for potential preclinical toxicology studies and clinical trials. The time and efforts required for us to fully establish manufacturing capabilities for our HtrA1 inhibitor program, including developing a viable manufacturing process, if any, may delay or impair our ability to develop this program in accordance with our expected timelines.

The manufacture of gene therapy products is complex with a number of scientific and technical risks, some of which are common to the manufacture of drugs and biologics and others of which are unique to the manufacture of gene therapies. We have limited experience with gene therapy manufacturing and are dependent on our third-party contract manufacturers and sole source suppliers.

Gene therapy drug products are complex and difficult to manufacture. We believe that the high demand for clinical gene therapy material and a scarcity of potential contract manufacturers may cause long lead times for establishing manufacturing capabilities for gene therapy drug development activities. Even after a manufacturer is engaged, any problems that arise during manufacturing process development may result in unanticipated delays to our timelines, including delays attributable to securing additional manufacturing slots. There may also be long lead times to manufacture or procure starting materials such as plasmids and cell lines, especially for high-quality starting materials that are cGMP compliant. In particular, plasmids, cell lines and other starting materials for gene therapy manufacture are usually sole sourced, as there are a limited number of qualified suppliers. The progress of our gene therapy programs is highly dependent on these suppliers providing us or our contract manufacturers with the necessary starting materials that meet our requirements in a timely manner. A failure to procure or a shortage of necessary starting materials likely would delay our manufacturing and development timelines.

A number of factors common to the manufacturing of biologics and drugs could also cause production issues or interruptions for gene therapies, including raw material or starting material variability in terms of quality, cell line viability, productivity or stability issues, shortages of any kind, shipping, distribution, storage and supply chain failures, growth media contamination, equipment malfunctions, operator errors, facility contamination, labor problems, natural disasters, disruption in utility services, terrorist activities, or acts of god that are beyond our or our contract manufacturer's control. It is often the case that early stage process development is conducted with materials that are not manufactured using cGMP starting materials,

techniques or processes and which are not subject to the same level of analysis that would be required for clinical grade material. We may encounter difficulties in translating the manufacturing processes used to produce research grade materials to cGMP compliant processes, and any changes in the manufacturing process may affect the safety and efficacy profile of our product candidates. In particular, we and our contract manufacturers are developing our own manufacturing processes, which differ from those originally used by our university collaborators, for example, by using different starting materials. We may not be able to successfully translate the manufacturing process and our manufactured materials may not match the safety and efficacy profile of those used by the universities.

An important part of manufacturing drug products is performing analytical testing. Analytical testing of gene therapies involves tests that are more numerous, more complex in scope and take a longer time to develop and to conduct as compared to traditional drugs. We and our contract manufacturers need to expend considerable time and resources to develop assays and other analytical tests for our gene therapy product candidates, including assays to assess the potency of our gene therapy product candidates. Some assays need to be outsourced to specialized testing laboratories. Even when assays are developed, they need to be further tested, qualified and validated, which may take substantial time and resources. Because of the lagging nature of analytical testing, we may proceed with additional manufacturing and other development activities without having first fully characterized our manufactured materials. If the results of the testing fail to meet our expectations, we may need to delay or repeat certain manufacturing and development activities.

In addition, because manufacturing for early stage research is often done under different conditions, using different starting materials and on a smaller scale than what is required for manufacturing for clinical supplies, we may face challenges in adapting the manufacturing processes that were used by our licensors and other academic collaborators and scaling up these processes as necessary to support supply for clinical trials. In order to progress the development of IC-100, IC-200 or any other gene therapy product candidate we may in-license or acquire, we will need to devote significant time and financial resources to establishing manufacturing processes that are sufficient for IND-enabling preclinical toxicology studies as well as clinical supplies. If we are not able to establish gene therapy manufacturing or related processes in a manner required for further development of our gene therapy product candidates, our development plans may be delayed or stalled and our business may be materially harmed.

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

The development and commercialization of new drug products is highly competitive. We face competition with respect to our product candidates and other programs from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies, as well as generic and biosimilar companies, worldwide. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. We also will face similar competition with respect to any product candidates that we may seek to develop or commercialize in the future.

We have transitioned to become a company with a focus on the development of gene therapies for orphan inherited retinal diseases. There are many companies pursuing gene therapy approaches for orphan and age-related retinal diseases. Some of them have better name recognition, more resources and a longer history of developing gene therapies than we do. Competition in this field is intense and for many inherited retinal diseases, there is a limited number of potential patients. If any of our competitors obtains FDA, EMA or other regulatory approval for their products more rapidly than we may obtain approval for ours, our competitors could establish a strong market position before we are able to enter the relevant market, which may significantly limit the commercial opportunity for our product candidates.

Our commercial opportunity could also be reduced or eliminated if one or more of our competitors develop and commercialize products that are more effective, safer, have fewer or less severe side effects, are more convenient to use or are less expensive than our product candidates. For example, the method of administration of Zimura, intravitreal injection, is commonly used to administer ophthalmic drugs for the treatment of severe diseases and is generally accepted by patients facing the prospect of severe visual loss or blindness. A therapy that offers a less invasive method of administration, however, might have a competitive advantage over one administered by intravitreal injection, depending on the relative safety of the other method of administration. Furthermore, our ability to compete may be affected in many cases by insurers or other third-party payors, particularly Medicare, seeking to encourage the use of less expensive or more convenient products.

In the case of orphan diseases such as the IRDs for which we are researching and developing potential treatments, should we be successful in development, our commercialization efforts may rely on non-patent market exclusivity periods under the Orphan Drug Act and the Hatch-Waxman Act. The Orphan Drug Act only provides exclusivity periods for the specific drug granted orphan drug designation for a specific indication. In addition, there are limited circumstances under each

of the Orphan Drug Act and the Hatch-Waxman Act that could result in our loss of data and marketing exclusivity, which could allow a competitor to enter the market. Failure to maintain either data or market exclusivity period could have a material adverse effect on our ability to commercialize our product candidates.

Many of our competitors have significantly greater financial and human resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient enrollment for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our development programs. Our timelines may be delayed to the extent clinical trials conducted by our competitors are enrolling patients that would otherwise be eligible to participate in our trials at the same time we are seeking to enroll these patients.

Based on publicly available information, we are aware of the following research and development programs that may be competitive with programs we are pursuing. Other competitive programs may exist of which we are not aware.

Competitive considerations for Dry AMD and GA:

- There are a number of products in preclinical research and clinical development by third parties to treat dry AMD, including several that are in development for GA secondary to dry AMD. In general, these product candidates can be categorized based on their proposed mechanisms of action. The mechanisms of action for these product candidates include complement system and inflammation suppression, visual cycle modulators, antioxidants and neuroprotectants, cell and gene therapies and vascular perfusion enhancers. We are aware that Apellis Pharmaceuticals, Inc., Roche AG, Novartis AG and MorphoSys AG, Hemera Biosciences, Inc., Gyroscope Therapeutics, Achillion Pharmaceuticals, Inc., and Catalyst Biosciences, Inc. each have complement inhibitors in development for dry AMD, including, in the cases of Hemera Biosciences and Gyroscope Therapeutics, complement inhibitor gene therapies. We believe that the most advanced of these programs is Apellis's pegylated, synthetic peptide targeting complement protein C3. As recently as November 2019, Apellis confirmed its expectation that it would finish patient enrollment in its Phase 3 program by the end of the first quarter of 2020, which would enable a primary 12-month efficacy analysis as early as the first half of 2021. If Apellis's Phase 3 program for its C3 complement inhibitor product candidate is successful, it is likely that Apellis would obtain marketing approval for its product candidate in advance of when we could reasonably expect marketing approval for Zimura in GA or a product candidate from our HtrA1 inhibitor program in GA, if at all. Moreover, we are aware that several other companies, including Allegro Ophthalmics, LLC and Stealth BioTherapeutics Corp, working in collaboration with Alexion Pharmaceuticals, Inc., have announced development programs for the treatment of dry AMD or GA targeting different mechanisms of action outside of the complement system.

Competitive considerations for Stargardt disease:

- There are a number of products in preclinical research and clinical development by third parties to treat Stargardt disease. We are aware that Sanofi, Acucela Inc., Alkeus Pharmaceuticals, Inc., Lin BioScience, Inc., Nightstar Therapeutics plc (prior to its acquisition by Biogen), ProQR Therapeutics N.V., Spark Therapeutics and Generation Bio Co. each have research or development programs in Stargardt disease. Three of these programs, Acucela, Alkeus and Lin BioScience, are exploring the use of oral therapeutics, while Sanofi, with technology provided by Oxford BioMedica plc, Nightstar and Spark are each using a gene therapy approach and ProQR is using an RNA based approach. Acucela’s product candidate is in Phase 3 development while Alkeus’s and Sanofi’s product candidates are each in Phase 2 development. Spark's program is in the research phase. In addition, several academic organizations have early stage programs in Stargardt disease.

Competitive considerations for RHO-adRP:

- We are aware that ProQR Therapeutics N.V. is developing an RNA-based therapeutic for RHO-adRP, for which it has filed an IND and plans to enroll patients this year. We are also aware that multiple academic institutions have early stage gene therapy development programs in RHO-adRP. In addition, prior to its acquisition by Biogen Inc., Nightstar Therapeutics plc had a preclinical AAV gene therapy program in RHO-adRP. Casebia Therapeutics LLP is pursuing research of a gene editing therapy for RHO-adRP. Editas Medicine, Inc. is also exploring a potential program in this disease.

Competitive considerations for BEST1-related IRDs:

- We are aware that, prior to its acquisition by Biogen, Nightstar Therapeutics plc had a preclinical AAV gene therapy program for one or more *BEST1*-related IRDs.

Competitive considerations for LCA10:

- We are aware that Editas Medicine has a CRISPR gene editing program for LCA10, an IND for which was submitted in late 2018, ProQR Therapeutics N.V. is developing an RNA-based therapeutic for LCA10 that is currently in late-stage clinical development, Generation Bio Co. has a preclinical program that utilizes ceDNA technology to target LCA10 and Oxford Biomedica plc is developing a lentiviral gene therapy program for LCA10 that is in preclinical development. In addition, several academic institutions have preclinical programs in LCA10.

Competitive considerations for USH2A-related IRDs*:*

- There are a number of products in preclinical research and clinical development by third parties to treat *USH2A*-related IRDs. We are aware that ProQR Therapeutics N.V. is pursuing two RNA based approaches for different mutations causing Usher 2A, one of which is currently in Phase 1/2 clinical development and the other of which is in preclinical development. We are also aware that Editas Medicine, Inc. and Odylia Therapeutics are exploring potential programs in *USH2A*-related IRDs.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing any of our product candidates that we develop if and when any such product candidate is approved.

As a company, we have no experience in the sale, marketing or distribution of pharmaceutical products. We currently do not have any sales, marketing or distribution infrastructure. To achieve commercial success for any approved product, we must either develop a sales, marketing and distribution organization or outsource those functions to third parties. We expect that our commercial strategy for any of our product candidates, including whether to retain commercial rights and market and sell the product candidate ourselves or to utilize collaboration, distribution or other marketing arrangements with third parties, would be determined based on a variety of factors, including the size and nature of the patient population, the disease area, the particular indications for which the product candidate is approved, the territories in which the product candidate may be marketed and the commercial potential for such product candidate. We are developing Zimura and our HtrA1 inhibitor program for GA secondary to dry AMD, which is a condition affecting a relatively large number of individuals. In contrast, our gene therapy programs are currently being developed for orphan IRDs with a limited number of affected individuals. If any of our product candidates is approved, the size and nature of the affected patient population will be an important factor in our commercial strategy. In addition, our commercial strategy would vary depending on whether the disease is typically treated by general ophthalmology practitioners, specialists, such as retinal specialists, or sub-specialists, such as retinal specialists with particular expertise in IRDs.

There are risks involved with establishing our own sales, marketing and distribution capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to adequate numbers of physicians who may prescribe our products;
- the lack of complementary products to be offered by our sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenues and our profitability, if any, are likely to be lower than if we were to market, sell and distribute ourselves any products that we develop. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we would not be successful in commercializing our product candidates, if approved.

Even if any of our product candidates receives marketing approval, such product candidate may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success and the market opportunity for any of our products and product candidates may be smaller than we estimate.

The degree of market acceptance of any product candidate that we are developing or we may develop, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments, including the existing standard of care;
- any restrictions in the label on the use of our products in combination with other medications or with certain devices;
- any restrictions in the label on the use of our products by a subgroup of patients, including, for example, for our gene therapy product candidates, if approved, restrictions on use of our product if a patient previously received another gene therapy product;
- restrictions in the label imposing a waiting period in between intravitreal or subretinal injections;
- our and any commercialization partner's ability to offer our products at competitive prices;
- availability of governmental and third-party payor coverage and adequate reimbursement;
- increasing reimbursement pressures on treating physicians due to the formation of accountable care organizations and the shift away from traditional fee-for-service reimbursement models to reimbursement based on quality of care and patient outcomes;
- willingness of the target patient population to try new therapies and of physicians to prescribe these therapies, particularly in light of the existing available standard of care or to the extent our product candidates require invasive procedures for administration, such as subretinal surgery;
- prevalence and severity of any side effects or perceived safety concerns, especially for new therapeutic modalities such as gene therapy; and
- whether competing products or other alternatives are more convenient or easier to administer, including whether co-formulated alternatives, alternatives that can be co-administered in a single syringe or alternatives that offer a less invasive method of administration than intravitreal injection or subretinal injection come to market.

Our development of Zimura for GA uses an anatomical primary endpoint, the mean rate of change in GA growth. We believe that this efficacy assessment is most likely to demonstrate clinical relevance for an investigational product across a heterogeneous GA patient population and other potential assessments, such as comparisons of visual acuity, are not as clinically meaningful for patients with GA. However, to date there is no direct functional equivalent to this endpoint that we are studying. We evaluated vision as a secondary endpoint in the OPH2003 trial, the trial was not designed to reliably assess differences in mean changes in vision with statistical significance. Patients, physicians and payors may not recognize the value of Zimura without us demonstrating a functional benefit to vision. To do so, we may need to identify and test using a suitable primary endpoint that is clinically relevant, which may not exist, or if it does exist, will involve additional clinical trials and uncertainty about the regulatory pathway for Zimura in GA.

For each of our Zimura trials where patients receive multiple intravitreal injections on the same day, we have provided for a delay in the second intravitreal injection to occur during the same office visit to minimize the risk of an unacceptable increase in intraocular pressure as a result of the volume of the multiple injections. If Zimura receives marketing approval for a particular indication and the approved label requires a waiting period between injections administered on the same day or a dosing regimen that requires multiple office visits per month, the potential market opportunity for Zimura may be limited to the extent that physicians and patients find such a waiting period or dosing regimen unacceptable. For example, if we proceed with and obtain marketing approval for a dosing regimen involving intravitreal injections of 4 mg of Zimura, consisting of two 2 mg injections per month, physicians and patients may find that treatment burden unacceptable.

In addition, the potential market opportunity for any product candidate is difficult to estimate precisely. Our estimates of the potential market opportunity for our product candidates include several key assumptions based on our expectations of the safety and effectiveness of the relevant product candidate, the expected patient population for our product candidates, our industry knowledge, the competitive landscape for the indications for which we are developing our product candidates and programs, market response to Spark Therapeutics's Luxturna®, Novartis AG's Zolgensma® and anti-VEGF agents currently approved for treatment of wet AMD, third-party research reports and other surveys. While we believe that our internal

assumptions are reasonable, no independent source has verified such assumptions and any of these assumptions could prove to be inaccurate, and the actual market for such product candidates could be smaller than our estimates of our potential market opportunity.

There are several factors that could contribute to the actual number of patients who receive an approved therapy being less than our current estimate of the potentially addressable market. With respect to our programs for orphan diseases, our understanding of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. These estimates may prove to be incorrect and new studies may reduce the estimated incidence or prevalence of these diseases. Further, the severity of the progression of a disease up to the time of treatment, especially in certain degenerative conditions such as IRDs, likely will diminish the therapeutic benefit conferred by a gene therapy due to irreversible cell death. Certain patients' immune systems and prior exposure to the virus used to deliver a gene therapy might inhibit the successful delivery of certain gene therapy products to the target tissue, thereby limiting eligibility for treatment or limiting treatment outcomes. If the number of patients that may benefit from the treatments we are seeking to develop is lower than we expect, our business, financial condition, results of operations and prospects may be adversely affected.

Even if we are able to commercialize any of the product candidates that we may develop, the product may become subject to unfavorable pricing regulations, pricing dynamics, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Health care reform, including increasing scrutiny of drug prices, is an issue of intense political focus, particularly in the United States. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals or in ways that could alter the mechanism by which pharmaceutical prices are negotiated or otherwise determined. Many countries outside the United States require approval of the sale price of a drug before it can be marketed, and to apply for and obtain such an approval in certain countries, we or a commercialization partner may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control or negotiation even after initial approval is granted. In particular for Zimura in GA, we may need to demonstrate visual function in order to obtain reimbursement approval, although our clinical trials, which use an anatomic endpoint as the primary efficacy endpoint, are not designed to demonstrate a functional benefit with statistical significance. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our or any commercialization partner's commercial launch of the product, possibly for lengthy time periods, which would negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval and are widely accepted and prescribed or used by physicians.

In addition, even in countries where pharmaceuticals are not subject to strict pricing regulations through a governmental review and approval process, we may nonetheless face an unfavorable pricing environment as a result of political pressure or market dynamics. Because there are only two FDA-approved gene replacement therapy products, one of which began commercial sales in 2018 and the other of which was only recently launched in the United States, the pricing environment for gene therapies is in the very early stages of its development. Gene therapies are generally intended to be one-time treatments or, at a minimum, to provide a benefit over an extended period lasting several years. If we are successful in obtaining marketing approval for any of our gene therapy product candidates, we will need to convince third-party payors of the value that our gene therapy product offers. Third-party payors may be unwilling to accept substantial upfront costs for a therapy where the benefits may not be realized or are realized over a period of years during which the patient may no longer be enrolled in the payor's plan. Although payors and manufacturers may be incentivized to agree to outcomes-based payment structures for gene therapies, where manufacturers provide rebates or a portion of the contract price is forgiven if an efficacy or durability threshold is not met for an individual patient, market dynamics in the United States currently do not facilitate these types of outcome-based payments, in particular because of rules that require that government payors, such as Medicaid, receive the "best price" for a drug, regardless of outcome. The perceived high cost for pharmaceutical products to treat orphan diseases, where manufacturers seek to recoup development costs and earn a profit for a therapy intended to treat a relatively small patient population, may attract increased political and public scrutiny. In particular, the $2.1 million list price for Zolgensma has generated significant public scrutiny over the prices of new pharmaceuticals coming to the market, including gene therapies, and as a result, Novartis has proposed permitting third-party payors to pay for Zolgensma in annual installments over five years instead of as a lump sum. Moreover, if we obtain marketing approval for a product candidate, such as Zimura, in more than one indication, including, for example in an orphan indication such as STGD1 and a non-orphan indication such as GA secondary to dry AMD, such a product candidate likely would only be sold at one price in any given country, regardless of the indications for

which it is prescribed. This dynamic may result in our charging a price that does not generate profits in each indication for which the product is approved.

Our ability and the ability of any commercialization partner to commercialize a product candidate successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A major trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors, particularly Medicare, have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications and encouraging the substitution of lower cost or generic products. Pricing pressures recently experienced by the pharmaceutical industry may be further exacerbated by legislative and policy changes under consideration by the Trump Administration and many states. For example, the Trump Administration, through the Center for Medicare & Medicaid Service, or CMS, announced in late 2018 an advance notice of proposed rulemaking describing a potential mandatory reference pricing model for Medicare Part B drugs under which the prices paid for these drugs will be adjusted in relation to an international pricing index that includes prevailing prices from other countries with strict price controls. CMS is considering issuing a proposed rule that would describe the model in more detail, with the goal of starting the model in spring 2020. The Trump Administration has also expressed an interest in authorizing and/or directing CMS or other agencies of the U.S. government to negotiate prices for drugs covered by Medicare directly with pharmaceutical companies. If this were to occur, especially for AMD drugs where a large portion of the patient population is over the age of 65 and is therefore covered by Medicare, there could be significant downward pressure on prices charged, not only for patients covered by Medicare, but also for patients covered by private insurers who may follow the government's lead on price. Moreover, increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for pharmaceutical products. We cannot be sure that coverage and reimbursement will be available for any product that we commercialize or any commercialization partner commercializes on our behalf, and, even if these are available, the level of reimbursement may not be satisfactory.

Reimbursement may affect the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be particularly difficult because of the higher prices often associated with drugs administered under the supervision of a physician. We or any commercialization partner may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies that may be on the market. If coverage and adequate reimbursement are not available or reimbursement is available only at limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside the United States. For example, several insurers have limited the subpopulation for or imposed additional eligibility criteria for paying for Zolgensma, beyond the requirements of the approved FDA label, such as requiring that any eligible patients must receive another treatment first and demonstrate that the other treatment is ineffective before using Zolgensma. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs, and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States, a policy that President Trump and certain members of the U.S. Congress have expressed interest in pursuing. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our and any commercialization partner's inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

For a further discussion of health care reform and other political factors affecting drug prices, see the risk factor herein entitled "*Current and future legislation and regulations may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we or they may charge for such products, when and if approved.*"

Ethical, legal and social issues related to genetic testing may reduce demand for any gene therapy product candidates we develop and for which we seek marketing approval.

We anticipate that prior to receiving certain gene therapies, including as part of a clinical trial, patients would be required to undergo genetic testing. Genetic testing has raised concerns regarding the appropriate utilization and the confidentiality of information provided by genetic testing. The ownership of genetic data is an area of the law that is unclear and varies across jurisdictions. Genetic tests for assessing a person's likelihood of developing a chronic disease have focused public attention on the need to protect the privacy of genetic information. For example, concerns have been raised that insurance carriers and employers may use these tests to discriminate on the basis of genetic information, resulting in barriers to the acceptance of genetic tests by consumers. This dynamic could lead to governmental authorities restricting genetic testing or calling for limits on or regulating the use of genetic testing, particularly for diseases for which there is no known cure, as well as the use of genetic data. Any of these scenarios could decrease the pool of patients willing to participate in a clinical trial for a gene therapy and the demand for a gene therapy once it is approved.

Product liability lawsuits against us or any future commercialization partner could divert resources, cause us to incur substantial liabilities and limit commercialization of any products that we may develop or in-license.

We face an inherent risk of product liability exposure related to the testing of any product candidate that we develop in human clinical trials, and we and any future commercialization partner will face an even greater risk if we commercially sell any products that we develop. If we become subject to or otherwise cannot successfully defend ourselves against claims that our product candidates or our products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop or in-license;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced time and attention of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop or in-license.

We currently hold $10.0 million in product liability insurance coverage in the aggregate, with a per incident limit of $10.0 million, which may not be adequate to cover all liabilities that we may incur. We will need to increase our insurance coverage when and if we begin commercializing an approved product. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise, including coverage for any local jurisdictions where we conduct clinical trials. In addition, if a commercialization or collaboration partner were to become subject to product liability claims or were unable to successfully defend themselves against such claims, any such commercialization or collaboration partners could be more likely to terminate such relationship with us and therefore substantially limit the commercial potential of our products.

Risks Related to Our Dependence on Third Parties

We contract with third parties for the manufacture of and for providing starting materials for our product candidates for preclinical development activities and clinical trials and expect to continue to do so in the future. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or product of sufficient quality, which could delay, prevent or impair our development or commercialization efforts.

We do not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of any of our product candidates and have a limited number of personnel hired to supervise outside contract manufacturers. We currently rely upon and expect to continue to rely upon third-party contract manufacturers to manufacture preclinical and clinical supplies of product candidates we are developing or may develop and commercial supplies of products if and when approved for marketing by applicable regulatory authorities. Furthermore, we and our contract manufacturers currently rely upon, and for the foreseeable future expect to continue to rely upon, sole-source suppliers of certain raw materials, plasmids and other specialized components of production used in the manufacture and fill/finish of our product candidates.

We currently rely exclusively upon, and purchase on a purchase order basis, a single third-party manufacturer to provide Zimura drug substance and a different single third-party manufacturer to provide fill/finish services for Zimura. We do not currently have any contractual commitments for the supply of Zimura drug substance. We also do not currently have arrangements in place for redundant supply or a second source for drug substance for Zimura or a second source for fill/finish services for Zimura. We purchase the polyethylene glycol, or PEG, reagent used to modify the chemically synthesized aptamer in Zimura on a purchase order basis from a single third-party supplier. We do not currently have any contractual commitments for supply of the PEG reagent we use for Zimura. The prices for manufacturing activities that are not yet contractually committed may vary substantially over time and adversely affect our financial results.

We have engaged a gene therapy CDMO for preclinical and Phase 1/2 clinical supply of IC-100 and IC-200. For our HtrA1 inhibitor program, we have engaged a CDMO to produce small quantities of the API for our HtrA1 inhibitors for preclinical development purposes and expect to engage a CDMO to conduct process development, scale-up and GMP manufacture of the API of our HtrA1 inhibitors for potential preclinical toxicology studies and clinical trials.

Our current and anticipated future dependence upon others for the manufacture of the product candidates that we are developing or may develop may adversely affect our business plan and future growth. For example, any performance failure or differing priorities on the part of our existing or future manufacturers could delay preclinical or clinical development or marketing approval of our product candidates. Our dependence on third party manufacturers may limit our ability to commercialize on a timely and competitive basis any products that receive marketing approval.

If any of our third-party manufacturers, fill/finish providers or sole-source suppliers fail to fulfill our purchase orders, or if any of these manufacturers or suppliers should become unavailable to us for any reason, including as a result of capacity constraints, differing priorities, regulatory compliance issues, financial difficulties or insolvency, we believe that there are a limited number of potential replacement manufacturers or sole source suppliers, and we likely would incur added costs and delays in identifying or qualifying such replacements. We may be unable to establish agreements with such replacement manufacturers, fill/finish providers or sole-source suppliers or to do so on acceptable terms.

In addition, to the extent that we or our third party manufacturers rely on materials that are sourced outside the United States, our supplier relationships could be interrupted due to international supply disruptions, including those caused by geopolitical and other issues. For example, trade disputes, trade negotiations or the imposition of tariffs between the United States and its trading partners could cause delays or disruptions in our supply of starting materials for our product candidates.

Reliance on third-party manufacturers entails additional risks, including:

- our product candidates may compete with other product candidates and products for access to a limited number of suitable manufacturing facilities that operate under cGMP conditions;
- reliance on the third party for regulatory compliance, quality assurance and quality control;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products and harm our business and results of operations.

We rely upon third parties in conducting our preclinical development activities and clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such activities.

We are relying upon and expect in the future to rely upon third parties, such as contract research organizations, or CROs, clinical data management organizations, biostatisticians, medical institutions (including reading centers) and clinical investigators, in conducting our preclinical testing and clinical trials for our product candidates. We or these third parties may terminate their engagements with us at any time for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, our product development activities could potentially be delayed and could potentially be very costly.

Our reliance on these third parties for preclinical testing and clinical development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with GCPs 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. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our preclinical studies or clinical trials in accordance with regulatory requirements or our stated protocols, we would not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and would not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. In particular, we rely upon the practices of and the systems in place at these third parties in conducting these studies and for quality control, and any failure of such practices or systems to comply with our stated protocols or regulatory requirements could adversely affect the quality of the data generated by these studies. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors.

We also rely upon other third parties to store, package, label and distribute drug supplies for our clinical trials and to store materials and drug substance for our preclinical development activities. Any performance failure on the part of these third parties could delay preclinical development, clinical development or marketing approval of our product candidates or commercialization of our products and adversely affect our results of operations.

We rely upon third-party researchers to advance our sponsored research programs. These arrangements may not ultimately yield any promising product candidates for preclinical or clinical development. We may not be able to fully realize the benefits of any intellectual property generated by these arrangements.

Part of our strategy involves collaborative sponsored research to be performed by third-party research institutions. Although we seek to direct this research and advise on the design of these projects as well as critical development decisions, this research is being performed by individuals who are not our employees and the timeline and quality of the research efforts are outside of our direct control. Academic investigators and other researchers may have different priorities than we do as a biopharmaceutical drug development company. The sponsored research agreements we enter into for these programs generally provide that any inventions resulting from the research will be owned by the research institution performing the research, and that we have an option to negotiate for a license to develop and exploit any such inventions. Confidential information and new inventions derived from these research efforts may be disclosed through publications or other means prior to our third-party research collaborators being able to protect such intellectual property through the filing of patent applications. Our third-party research collaborators may not be able to obtain or maintain full ownership of inventions that are derived from the research or associated rights, which may limit their ability to provide us with a license to all relevant intellectual property on terms and conditions that are acceptable to us. Even if our collaborative research efforts yield promising results or new technological advances, they may not ultimately result in our being able to protect, develop or exploit the resulting intellectual property.

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

The development and potential commercialization of our product candidates is likely to require substantial additional cash to fund expenses. In addition, the commercialization of a product candidate in markets outside of the United States requires regulatory expertise and commercial capabilities that are specific to the local market. For some of our product candidates, we may seek to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. In particular, we are exploring seeking collaboration opportunities for the further development and potential commercialization of Zimura.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a 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 candidate. For a number of our product candidates, we are party to in-license agreements that limit who we can collaborate with or require the approval of our licensor for us to enter into a collaboration,

and any future license agreements that we may enter into may have similar restrictions. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among pharmaceutical and biotechnology 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 those product candidates or bring them to market and generate product revenue.

If we enter into collaborations with third parties for the development or commercialization of our product candidates, any such collaborations will carry numerous risks. If any of our collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We may utilize a variety of types of collaboration, distribution and other marketing arrangements with third parties to develop or commercialize our product candidates, either in the United States, or in markets outside the United States. We also may seek third-party collaborators for development and commercialization of other product candidates we may develop. Our likely collaborators for any sales, marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. If we do enter into any additional arrangements with third parties in the future, we would likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates could pose numerous risks to us, including the following:

- collaborators, including marketing and distribution collaborators, have significant discretion in determining the efforts and resources that they will apply to these collaborations and may not perform their obligations as expected;
- collaborators may deemphasize or not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus, changes in product candidate priorities or available funding or changes in priorities as a result of a merger, acquisition or other corporate restructuring or transaction;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- we could grant exclusive rights to our collaborators, which would prevent us from collaborating with others;
- disagreements or disputes with collaborators, including disagreements or disputes over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of products or product candidates, might lead to additional responsibilities for us with respect to product candidates or might result in litigation or arbitration, any of which would divert management attention and resources, be time-consuming and be expensive;
- collaborators may not properly maintain or defend our intellectual property rights, may infringe the intellectual property rights of third parties, may misappropriate our trade secrets or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator, our breach of the terms of the collaboration or other reasons and, if terminated, we may need to raise additional capital to pursue further development or commercialization of the applicable product candidates.

If a collaborator of ours were to be involved in a business combination or other transaction, the foregoing risks would be heightened, and the business combination or transaction may divert attention or resources or create competing priorities. The collaborator may delay or terminate our product development or commercialization program. If one of our collaborators terminates its agreement with us, we could find it more difficult to attract new collaborators and the perception of our company could be adversely affected.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

We depend on licenses and sublicenses for development and commercialization rights to Zimura, IC-100, IC-200 and our miniCEP290 program. These license arrangements, as well as the Inception 4 Merger Agreement, impose diligence obligations on us. We may enter into similar arrangements with respect to future product candidates or technologies. Termination of licenses or the failure by us or our licensees, including our potential future commercialization or collaboration partners, to comply with obligations under these or other agreements could materially harm our business and prevent us from developing or commercializing our products and product candidates.

We are party to a license agreement with Archemix on which we depend for rights to Zimura. We are party to two different license agreements, each with UFRF and Penn, on which we depend for rights to IC-100 and IC-200. We are also party to a license agreement with UMMS for our miniCEP290 program. These agreements generally impose diligence, development and commercialization timelines, milestone payment, royalty, insurance and other obligations on us. Generally, the diligence obligations contained in these agreements require us to use commercially reasonable efforts to develop, seek regulatory approval for and commercialize the applicable product candidate in the United States and certain territories outside of the United States, including the European Union, Japan and such other markets where it would be commercially reasonable to do so. Under the license agreements for our product candidates, we would not be able to avoid our payment obligations even if we believed a licensed patent right was invalid or unenforceable because the license agreements provide that our licenses to all licensed patent rights would terminate if we challenge the validity or enforceability of any licensed patent right. The Inception 4 Merger Agreement, pursuant to which we acquired our HtrA1 inhibitor program, also imposes specified diligence and milestone payment obligations on us. We may enter into acquisition or licensing agreements in the future that would impose similar obligations on us.

If we fail to comply with our obligations under current or future acquisition and licensing agreements, or otherwise breach an acquisition or licensing agreement as a result of our own actions or inaction or the actions or inactions of our commercialization or collaboration partners, our counterparties may have the right to terminate these agreements, in which event we might not have the rights or the financial resources to develop, manufacture or market any product that is covered by these agreements. Our counterparties also may have the right to convert an exclusive license to non-exclusive in the territory in which we fail to satisfy our diligence obligations, which could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or restated agreements with less favorable terms, seek alternative sources of financing or cause us to lose our rights under these agreements, including our rights to Zimura, IC-100, IC-200, our miniCEP290 program, and other important intellectual property or technology. Any of the foregoing could prevent us from commercializing our product candidates, which could have a material adverse effect on our operating results and overall financial condition. In the case of our limited diligence obligation under the Inception 4 Merger Agreement, a potential breach of our obligation to use commercially reasonable efforts to develop an HtrA1 inhibitor could lead to a lawsuit with the former equityholders of Inception 4 and result in potential liability to us of up to $5 million.

In addition to the above risks, certain of our intellectual property rights are sublicenses under intellectual property owned by third parties, in some cases through multiple tiers. The actions of our licensors may therefore affect our rights to use our sublicensed intellectual property, even if we are in compliance with all of the obligations under our license agreements. Should our licensors or any of their upstream licensors fail to comply with their obligations under the agreements pursuant to which they obtain the rights that are sublicensed to us, or should such agreements be terminated or amended, our ability to develop and commercialize the relevant product candidates may be materially harmed. While the applicable agreements may contain contractual provisions that would in many instances protect our rights as a sublicensee in these circumstances, these provisions may not be enforceable and may not protect our rights in all instances. Further, we do not have the right to control the prosecution, maintenance and enforcement of all of our licensed and sublicensed intellectual property, and even when we do have such rights, we may require the cooperation of our licensors and their upstream licensors, which may not be forthcoming. Our business could be materially adversely affected if we are unable to prosecute, maintain and enforce our licensed and sublicensed intellectual property effectively.

Moreover, the license agreements for IC-100, IC-200 and our miniCEP290 program reserve for the licensing academic institutions the right to continue to practice for research purposes, the inventions covered by the intellectual property rights that we have in-licensed. These licensing institutions or their collaborators may generate scientific, preclinical or clinical data with

respect to our product candidates, separate from our research and development efforts, that is inconsistent with other data for such product candidates, including additional preclinical and clinical data that we develop. Investigators at these institutions may publish, present, or otherwise publicly disclose this data, which may have an adverse impact on the prospects of the development of our product candidates and may harm our business. In addition, these institutions may use these data to support new patent applications which could result in the issuance of patents that may limit our freedom to operate without our obtaining additional licenses to these newly developed inventions.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain or do not maintain patent protection for our technology and products, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be adversely affected.

We currently rely and expect to continue to rely on patent rights to protect our competitive position. Once our patents expire, we may not be able to exclude competitors from commercializing products similar or identical to ours. The U.S. patent rights covering Zimura as a composition of matter are expected to expire in 2025. The U.S. patent rights covering methods of treating certain complement protein mediated disorders with Zimura are expected to expire in 2026. The European patent rights covering the composition of matter of Zimura and methods of treating certain complement protein mediated disorders with Zimura are expected to expire in 2025. We expect the clinical development of Zimura to continue for at least the next several years. If so, the patents covering Zimura may expire before the date by which we or a potential commercial partner would be able to commercialize Zimura in the United States or Europe if we seek and obtain marketing approval. Even if we are able to obtain marketing approval for and commercially launch Zimura prior to the expiration of these patents, the remaining term of those patents may be shorter than we anticipate. Although the patent rights under existing patent applications for IC-100, our miniCEP290 program and our HtrA1 inhibitors are not expected to expire until 2037 or after, we face the same risk with those product candidates and programs and any future product candidates that we may develop.

Our product candidate IC-200 is not currently covered by a patent or pending patent application. In developing and advancing this product candidate, we may seek to rely on the prospect of generating new intellectual property during development of the product candidate or the potential for non-patent market exclusivity, including regulatory exclusivity as a result of the Orphan Drug Act. If we, together with Penn and UFRF, are unable to generate data to support a patent or patent application to cover this product candidate or if we are unable to obtain non-patent market exclusivity, we may not be able to exclude competitors from marketing an identical or substantially similar product.

For our sponsored research agreements with UMMS and Penn, we are generally relying on our university collaborators to generate research and data to support new patent applications. The results of any sponsored research are uncertain and the interests of the universities and university researchers are not necessarily aligned with our interests as a commercial entity. The research may generate limited patentable results or data, or none at all. Furthermore, the universities generally control the filing, prosecution and maintenance of any patents or patent applications resulting from the sponsored research. Therefore, we may not be able to obtain any patent or other exclusivity protections as a result of our collaborative gene therapy sponsored research programs, which could materially diminish or eliminate the value of these programs.

Certain of our licensed patent rights for Zimura and IC-100 are method-of-treatment patents. Method-of-treatment patents are more difficult to enforce than composition-of-matter patents because of the risk of off-label sale or use of a drug for the patented method. The FDA does not prohibit physicians from prescribing an approved product for uses that are not described in the product's labeling. Although use of a product directed by off-label prescriptions may infringe our method-of-treatment patents, the practice is common across medical specialties, particularly in the United States, and such infringement is difficult to detect, prevent or prosecute. Off-label sales of other products having the same drug substance as Zimura or any other product candidates we may develop would limit our ability to generate revenue from the sale of Zimura or such other product candidates, if approved for commercial sale. In addition, European patent law generally makes the issuance and enforcement of patents that cover methods of treatment of the human body difficult. Further, once the composition-of-matter patents relating to Zimura or any other product candidate in a particular jurisdiction, if any, expire, competitors will be able to make, offer and sell products containing the same drug substance as Zimura or such other product candidate in that jurisdiction so long as these competitors do not infringe any of our other patents covering Zimura's composition of matter or method of use or manufacture, do not violate the terms of any marketing or data exclusivity that may be granted to us by regulatory authorities and they obtain any necessary marketing approvals from applicable regulatory authorities. In such circumstances, we also may not be able to detect, prevent or prosecute off-label use of such competitors' products containing the same drug substance as Zimura, even if such use infringes any of our method-of-treatment patents.

Depending on potential delays in the regulatory review process for any of our product candidates, we may be able to obtain patent term extension for one of our patents in the United States under the Hatch-Waxman Act, which permits a patent

extension term of up to five years as partial compensation for patent term effectively lost during product development and the FDA regulatory review process occurring after the issuance of a patent, but we can provide no assurances that such an extension term will be obtained. Similar to the patent term extension available in the United States, the regulatory framework in the European Union and certain other foreign jurisdictions provides the opportunity to extend the term of a patent that covers an approved drug in certain circumstances. Notwithstanding the availability of patent term extension provisions, we may not be granted patent term extensions 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, such as using diligent efforts to develop a drug candidate. 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 the term or scope of any such extension is less than we request, any period during which we have the right to exclusively market our product would be shorter than we would otherwise expect, and our competitors may commercialize competing products following our patent expiration, and our revenue could be reduced, possibly materially.

The Hatch-Waxman Act also permits the manufacture, use, offer for sale, sale or importation of a patented invention other than a new animal drug or veterinary biological product, if the manufacture, use, offer for sale, sale or importation is solely for uses that are reasonably related to development of information that could be submitted to the FDA. For this reason, our competitors might be able under certain circumstances to perform activities within the scope of the U.S. patents that we own or under which we are licensed without infringing such patents. This might enable our competitors to develop during the lifetime of these patents drugs that compete with our product candidates.

Our issued patents may not be sufficient to provide us with a competitive advantage. For example, competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. Even if our owned or licensed patent applications issue as patents, they may not issue with a scope broad enough to provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage.

The issuance of a patent is not conclusive as to its inventorship, ownership, scope, term, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. For example, if we receive marketing approval for our product candidates, other pharmaceutical companies may seek approval of generic or biosimilar versions of our products with the FDA or regulatory authorities in other jurisdictions. We may then be required to initiate proceedings against such companies in order to enforce our intellectual property rights. The risk of being involved in such proceedings is likely to increase if our products are commercially successful. In any such proceedings, the inventorship, ownership, scope, term, validity and enforceability of our patents may be challenged. These and other 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 prevent others from using or commercializing similar or identical technology and products or from launching generic or biosimilar versions of our products, or could limit the duration of the patent protection of our technology and products. The launch of a generic version of one of our products in particular would be likely to result in an immediate and substantial reduction in the demand for our product, which could have a material adverse effect on our business. 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. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

The patent prosecution process is expensive and time-consuming, is highly uncertain and involves complex legal and factual questions. Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products. We seek to protect our proprietary position by filing in the United States and in certain foreign jurisdictions patent applications related to our novel technologies and product candidates that are important to our business.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. In addition, we may not pursue or obtain patent protection in all major markets. Moreover, in some circumstances, we do not have the right to control the preparation, filing or prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties or covering technology that a collaboration or commercialization partner may develop, the eventual commercialization of which could potentially entitle us to royalty payments. In some circumstances, our licensors may have the right to enforce the licensed patents without our involvement or consent, or to decide not to enforce or to allow us to enforce the licensed patents. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. If any such licensors fail to maintain such patents, or lose rights to those patents, the rights

that we have licensed may be reduced or eliminated and our ability to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign jurisdictions may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions. Moreover, the U.S. Patent and Trademark Office, or USPTO, might require that the term of a patent issuing from a pending patent application be disclaimed and limited to the term of another patent that is commonly owned or names a common inventor. As a result, the issuance, scope, validity, term, enforceability and commercial value of our patent rights are highly uncertain.

Our pending and future patent applications, and any collaboration or commercialization partner's pending and future patent applications, may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. In particular, during prosecution of any patent application, the issuance of any patents based on the application may depend upon our or their ability to generate additional preclinical or clinical data that support the patentability of our proposed claims. We or any collaboration or commercialization partner may not be able to generate sufficient additional data on a timely basis, or at all. Moreover, changes in either the patent laws or interpretation of the patent laws in the United States or other countries may diminish the value of our or a collaboration or commercialization partner's patents or narrow the scope of our or their patent protection.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. The Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law in September 2011, and many of the substantive changes became effective in March 2013. The Leahy-Smith Act revised United States patent law in part by changing the standard for patent approval from a "first to invent" standard to a "first to file" standard and developing a post-grant review system. This legislation changed United States patent law in a way that may weaken our ability to obtain patent protection in the United States for those applications filed after March 2013. For example, if we are the first to invent a new product or its use, but another party is the first to file a patent application on this invention, under the new law the other party may be entitled to the patent rights on the invention.

Moreover, we may be subject to a third-party preissuance submission of prior art to the USPTO, or become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review, interference proceedings or other patent office proceedings or litigation, in the United States or elsewhere, challenging our patent rights or the patent rights of others. The Leahy-Smith Act expanded the ability of third parties to challenge the patents held by patentees through administrative reviews at the USPTO, which may facilitate others to challenge our patents. Based on available information, we believe that *inter partes* review proceedings, brought by financial investors who may be selling short the stock of the patent holder, are becoming more prevalent. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights; allow third parties to commercialize our technology or products and compete directly with us, without payment to us; or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to develop or commercialize current or future product candidates.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe or otherwise violate our patents, trademarks, copyrights or other intellectual property. To counter infringement or other violations, we may be required to file claims, which can be expensive and time consuming. For some of our licensed patent rights, we may need the cooperation of our licensors to file such claims. Any such claims could provoke these parties to assert counterclaims against us, including claims alleging that we infringe their patents or other intellectual property rights. In addition, in a patent infringement proceeding, a court may decide that one or more of the patents we assert is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to prevent the other party from using the technology at issue on the grounds that our patents do not cover the technology. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In such a case, we could ultimately be forced to cease use of such marks. In any intellectual property litigation, even if we are successful, any award of monetary damages or other remedy 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 this type of litigation.

Third parties may initiate legal proceedings or take other actions alleging that we are infringing or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of any future collaboration and commercialization partners to develop, manufacture, market and sell our product candidates and products and use our proprietary technologies without infringing or otherwise violating the intellectual property and other proprietary rights of third parties. New patent applications in the field of biotechnology and pharmaceuticals, and gene therapies in particular, are being filed at a rapid pace.

There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. We or any future collaboration and commercialization partners may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference, derivation, re-examination, post-grant review, *inter partes* review, opposition, cancellation or similar proceedings before the USPTO or its foreign counterparts. The risks of being involved in such litigation and proceedings may increase as our product candidates near commercialization.

Third parties may assert infringement or other claims against us or our collaboration or commercialization partners based on existing or future intellectual property rights. We or they may not be aware of all such intellectual property rights potentially relating to our product candidates and their manufacture and uses. In addition, contract manufacturers may inadvertently incorporate intellectual property belonging to third parties into our products or the manufacturing processes for these products without our knowledge. There is a lag between the filing of a patent application, which generally establishes the priority date of a patent claim, and the publication of such patent application. During the period between filing of a patent application and publication of the application, we would not otherwise have a means of discovering the existence or extent of the claimed inventions contained in a filed but unpublished patent application. Patent applications are often drafted broadly, and the scope of patent claims that may ultimately issue may not be known until several years after a patent application is filed and published. We may make development or pipeline decisions based on our belief that our product candidates can be distinguished from patent claims contained in published patent applications or issued patents, that patent claims contained in published patent applications are unlikely to issue as drafted, or that claims contained in issued patents are invalid. These positions regarding third-party intellectual property may not ultimately be successful in litigation. Thus, we do not know with certainty that our product candidates, or our intended commercialization thereof, does not and will not infringe or otherwise violate any third party's intellectual property.

If we are or any of our future collaboration or commercialization partners is found to infringe or otherwise violate a third party's intellectual property rights, we or they could be required to obtain a license from such third party to continue developing and marketing our product candidates or products or to continue using a trademark. However, we or our future collaboration and commercialization partners may not be able to obtain any required license on commercially reasonable terms or at all. Even if we or they were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us or our collaboration and commercialization partners and could require us or them to make substantial licensing and royalty payments. We or our future collaboration and commercialization partners could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us or our future collaboration and commercialization partners from commercializing our product candidates or force us or them to cease some of our business operations, which could materially harm our business. Claims that we or our future collaboration and commercialization partners have misappropriated the confidential information or trade secrets of third parties could expose us or them to similar liabilities and have a similar negative impact on our business.

We may be subject to claims by third parties asserting that we or our employees or contractors have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees and contractors were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees and contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees or contractors have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's or contractor's former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or 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 conceives or develops intellectual property that we regard as our own. Moreover, because we acquired rights to our product candidates from third parties, we must rely upon these third parties'

practices, and those of their predecessors, with regard to the assignment of intellectual property therein, including the intellectual property rights protecting the HtrA1 inhibitors we acquired in the Inception 4 acquisition transaction. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our 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 or personnel.

Intellectual property litigation could cause us to spend substantial resources and could distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. 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 substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. 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.

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

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and patent offices in foreign countries in several stages over the lifetime of the patent. The USPTO and patent offices in foreign countries require compliance with a number of procedural, documentary, fee payment and other requirements during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of a patent or patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market sooner than we expect, which would have a material adverse effect on our business.

In addition, we may decide not to pursue patent prosecution in certain major markets or jurisdictions. For example, we may decide that the costs of obtaining and maintaining patent protection in a certain jurisdiction may outweigh the commercial benefits of patent protection. If so, our competitors may enter into and commercialize identical or similar products in that jurisdiction and if we choose to commercialize our products in that jurisdiction, we may not be able to exclude our competitors in the same way as if we had chosen to pursue patent prosecution in that jurisdiction.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and products, we also rely upon trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our outside scientific collaborators, contract manufacturers, potential business development counterparties, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. We cannot guarantee that we have executed such agreements with each party that may have or have had access to our trade secrets. Moreover, because we acquired our HtrA1 inhibitor program through the acquisition of Inception 4, we are relying upon Inception 4's, and its prior owner's, practices with regard to the protection of trade secrets and intellectual property rights for the period prior to our acquisition of Inception 4. Any party with whom we or they have executed a non-disclosure and confidentiality agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Our proprietary information may also be obtained by third parties by other means, such as breaches of our physical or computer security systems.

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 and our competitive position would be harmed.

Risks Related to Information Technology

We rely significantly upon information technology systems and any failure, inadequacy, interruption or security lapse of these systems could harm our ability to operate our business effectively.

In the ordinary course of our business, we and our third-party contractors maintain personal and other sensitive data on our and their respective networks, including our intellectual property and proprietary or confidential information relating to our business and that of our clinical trial participants, business collaborators and employees. In particular, we rely on contract research organizations and other third parties to store and manage data generated from our preclinical research and development activities and information from our clinical trials. The secure maintenance of this sensitive information is critical to our business and reputation.

We have implemented a number of measures to protect our information technology systems. These measures include, among others, creation of a cyber-security governance team and standard operating procedures for responding to any cyber-security incidents, mandatory cyber-security training for our employees and consultants with access to our information technology systems and engagement of a third-party vendor to assess our informational technology systems and potential vulnerabilities.

Despite the implementation of security measures, our internal computer systems and those of our third-party contractors are vulnerable to compromise, damage, loss or exfiltration from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. In particular, companies and other entities and individuals have been increasingly subject to a wide variety of security incidents, cyber-attacks, phishing scams and other attempts to gain unauthorized access to systems and information, including through social engineering. The number and complexity of these threats continue to increase over time. These threats can come from a variety of sources, ranging in sophistication from individual hackers to state-sponsored attacks. Cyber threats may be broadly targeted, or they may be custom-crafted against our information systems or those of our third-party contractors.

For information stored with our third-party contractors, we rely upon, and the integrity and confidentiality of such information is dependent upon, the risk mitigation efforts such third-party contractors have in place. Cyber-attacks have become more prevalent and much harder to detect and defend against. Our and our third-party contractors' respective network and storage applications may be subject to unauthorized access by hackers or breached due to operator error, malfeasance or other system disruptions. We might not anticipate or immediately detect such incidents and the damage caused by such incidents. System failures, data breaches and any unauthorized access or disclosure of our information or intellectual property could compromise our intellectual property and expose sensitive business information. System failures or accidents or security breaches could cause interruptions in our operations, and could result in a material disruption of our research and development activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. Moreover, if a breach of our security or that of our vendors occurs, the market perception of the effectiveness of our security measures could be harmed and our reputation could be damaged.

A data security breach could also lead to public or unauthorized exposure of personal information of our clinical trial participants, our employees or others. Cyber-attacks and the measures we implement to prevent, detect, and respond to them could cause us to incur significant remediation costs, result in product development delays, disrupt key business operations, expose us to contractual damages and/or regulatory liability, require us to make certain breach notifications, divert the attention of our management and key information technology resources, harm our reputation and deter patients, clinical investigators or other business collaborators from participating in our clinical trials or otherwise working with us. Any loss of preclinical data or clinical trial data 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 public disclosure of confidential or proprietary information, we could incur liability and our product development and commercialization efforts could be delayed. In addition, we may not have adequate insurance coverage to provide compensation for any losses associated with such events.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union,

including personal health data, is subject to the EU General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party data processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Given the breadth and depth of changes in data protection obligations, preparing for and complying with the GDPR's requirements has required and will continue to require significant time, resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. We are aware that several states have enacted or are considering legislation similar to the GDPR. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices, and any non-compliance by us or our employees, consultants or contractors could lead to government enforcement actions, private litigation, significant fines and penalties, or reputational harm and could have a material adverse effect on our business, financial condition or results of operations.

Risks Related to Regulatory Approval and Marketing of our Product Candidates and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue would be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution and import and export, are subject to comprehensive regulation by the FDA, the EMA and comparable regulatory agencies in other countries.

In general, the FDA and similar regulatory authorities outside the United States require two adequate and well-controlled clinical trials demonstrating safety and effectiveness for marketing approval for an ophthalmic pharmaceutical product. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely upon third-party CROs to assist us in this process. Securing marketing approval requires obtaining positive safety and efficacy data from required clinical trials, as well as the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing processes to, and inspection of manufacturing facilities by, the relevant regulatory authorities. The FDA or other regulatory authorities may determine that a product candidate that we may develop is not effective, is only moderately effective or has undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Marketing approval of novel product candidates such as Zimura and our gene therapy product candidates manufactured using novel manufacturing processes can be more expensive and take longer than for other, more well-known or extensively studied pharmaceutical or biopharmaceutical products, due to regulatory agencies' lack of experience with them. We believe that the FDA has only granted marketing approval for one aptamer product and two gene replacement products to

date. This lack of experience may lengthen the regulatory review process, require us to conduct additional studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these product candidates or lead to significant post-approval limitations or restrictions.

Accordingly, if we or our collaborators experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for such product candidate may be harmed and our ability to generate revenues would be materially impaired.

For a further discussion of the requirements for regulatory approval of Zimura in GA, see the section in the Management's Discussion and Analysis of Financial Condition and Results of Operations entitled "Requirements for Regulatory Approval of Zimura in GA."

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed in such jurisdictions. The approval requirements in foreign jurisdictions may differ significantly from those in the United States.

In order to market and sell our product candidates in the European Union and many other jurisdictions, we or our third-party commercialization partners must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional preclinical or clinical testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or our third-party commercialization partners may not obtain marketing and/or reimbursement approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We and our third-party commercialization partners may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Additionally, in June 2016 the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. The process for withdrawal has been and remains uncertain and convoluted, with the United Kingdom currently scheduled to withdraw from the European Union on January 31, 2020, and currently, no effective withdrawal agreement has been concluded between the European Union and the United Kingdom. The United Kingdom will conduct a general parliamentary election on December 12, 2019, which will determine how, if at all, Brexit occurs. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, Brexit could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business. It remains to be seen how, if at all, Brexit will actually occur and how, if at all, Brexit will impact regulatory requirements for the approval of pharmaceutical product candidates and the sale of pharmaceutical products in the United Kingdom and the European Union.

A fast track designation or grant of priority review status by the FDA may not actually lead to a faster development or regulatory review or approval process. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

The FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and if the product demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a fast track product’s application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA’s time period goal for reviewing a fast track application does not begin until the last section of the application is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

The FDA has broad discretion whether or not to grant fast track designation or priority review status, so even if we believe a particular product candidate is eligible for such designation or status the FDA could decide not to grant it. Even

though a product has received fast track designation and may be eligible for priority review status, a sponsor may not ultimately experience a faster development process, review or approval compared to conventional FDA procedures.

A breakthrough therapy designation by the FDA for our product candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates would receive marketing approval.

In 2012, Congress enacted the Food and Drug Administration Safety and Innovation Act, or FDASIA. This law established a new regulatory scheme allowing for expedited review of products designated as "breakthrough therapies." A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead decide not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not ensure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification or that the time period for FDA review or approval will not be shortened.

We currently do not have orphan drug designations or orphan drug exclusivity for any product candidate. If our competitors are able to obtain orphan drug exclusivity for products that constitute the same drug and treat the same indications as our product candidates, we may not be able to have our product candidates approved by the applicable regulatory authority for a significant period of time.

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as having a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the European Union, the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than 5 in 10,000 persons in the European Union. Additionally, orphan designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biologic product.

If we request orphan drug designation for any of our product candidates in one or more indications, there can be no assurances that the FDA or the European Commission will grant any of our product candidates such designation. Additionally, the designation of any of our product candidates as an orphan product does not guarantee that any regulatory agency will accelerate regulatory review of, or ultimately approve, that product candidate, nor does it limit the ability of any regulatory agency to grant orphan drug designation to product candidates of other companies that treat the same indications as our product candidates prior to our product candidates receiving exclusive marketing approval.

Generally, if a product candidate with an orphan drug designation receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the European Commission during that marketing exclusivity period from approving another marketing application for a product that constitutes the same drug treating the same indication, except in limited circumstances. If another sponsor receives such approval before we do, regardless of our orphan drug designation, we will be precluded from receiving marketing approval for our product candidate during the applicable exclusivity period. The applicable period is seven years in the United States and 10 years in the European Union. The exclusivity period in the United States can be extended by six months if the sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The exclusivity period in the European Union can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be revoked if any regulatory agency determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different drugs can be approved for the same condition. In the United States, even after an orphan drug is approved, the FDA may subsequently approve another drug for the same condition if the FDA concludes that the later drug is not the same drug or is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In particular, the concept of what constitutes the "same drug" for purposes of orphan drug exclusivity is unclear in the context of gene therapies, and the FDA has issued draft guidance suggesting minor variations in the construct of a gene therapy that lead to improvements in safety or efficacy may result in the determination that a drug is a "different drug". In the European Union, marketing authorization may be granted to a similar medicinal product for the same orphan indication if:

- the second applicant can establish in its application that its medicinal product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior;
- the holder of the marketing authorization for the original orphan medicinal product consents to a second orphan medicinal product application; or
- the holder of the marketing authorization for the original orphan medicinal product cannot supply sufficient quantities of the orphan medicinal product.

Any product candidate for which we obtain marketing approval could be subject to post-marketing restrictions or withdrawal from the market and we or our third-party commercialization partners may be subject to penalties if we or our third-party commercialization partners or our or their manufacturers fail to comply with regulatory requirements or if we or our third-party commercialization partners or our or their manufacturers experience unanticipated problems with our products, when and if any of them are approved.

Any product candidate for which we or our commercialization partners obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to the continued requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control and quality assurance, complaints and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or may be subject to significant conditions of approval or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine, including the requirement to implement a risk evaluation and mitigation strategy.

The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on distribution or use of a product;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;

- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions or the imposition of civil or criminal penalties; and
- litigation involving patients using our products.

Non-compliance with European Union requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties.

Our and our potential commercialization partners' relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us and our commercialization partners to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with healthcare providers, physicians and third-party payors may expose us and our commercialization partners to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we and our commercialization partners market, sell and distribute any products for which we or they obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or *qui tam* actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at a minimum of $10,781 and a maximum of $20,563 per false claim;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act requires certain manufacturers of drugs, medical devices and biological products covered by federal healthcare benefit programs to report payments and other transfers of value to physicians and teaching hospitals; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and transparency statutes, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by governmental and non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws, such as the GDPR, also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

If our operations are found to be in violation of any of the laws described above or any governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our financial results. As our product candidates advance in clinical development, we plan to develop and implement a corporate compliance program to ensure that we will market and sell any future products that we successfully develop in compliance with all applicable laws and regulations, but we cannot guarantee that any such program will protect us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws and regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

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 governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our or our commercialization partners' operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us or them, we or they may be subject to significant civil, criminal and administrative penalties, including damages, fines, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our or their operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Our operations may be dependent on the normal function of the FDA, the SEC and other government agencies. The inability of those agencies to obtain necessary funding and other effects from the political process could prevent those agencies from performing normal functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new product applications such as INDs, new drug applications and biologics license applications can be affected by a variety of factors, including government funding levels, ability to hire and retain key personnel and to accept the payment of user fees, and statutory, regulatory, and policy changes. Government funding of the FDA, the SEC and other government agencies on which our operations may rely is subject to the political process, which is inherently fluid and unpredictable. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations. In addition, the Trump Administration has taken several executive actions, including the issuance of a number of executive orders, that could affect federal agencies, including the FDA. Those executive actions, some of which are still being implemented, may impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities, which could negatively impact our business.

Current and future legislation and regulations may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we or they may charge for such products, when and if approved.

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, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may charge for any approved products.

In March 2010, President Barack H. Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA. Among the provisions of the ACA of potential importance to our business and our product candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription products and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;

- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer, originally 50% and as of 2019, 70%, point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report product samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2025 unless additional congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

Since enactment of the ACA, there have been numerous legal challenges and congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, Congress repealed the "individual mandate." The repeal of this provision, which required most Americans to carry a minimal level of health insurance, became effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Further, the Bipartisan Budget Act of 2018, among other things, amended the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." Congress may consider other legislation to amend or replace elements of the ACA during the current congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA, which has lead to numerous legal challenges to the ACA and the Trump Administration's actions. Since January 2017, President Trump has signed at least two executive orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One executive order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. A second executive order terminated the cost-sharing subsidies that reimburse insurers under the ACA, which has lead some states attorneys general and some insurers to sue the Trump Administration for such payments and a number of those lawsuits remain pending. Further, in June 2018, the U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued the payments were owed to them, which the U.S. Supreme Court plans to review during its current term. In addition, in October 2018 CMS promulgated regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.

We will continue to evaluate the effect that the ACA, its possible amendment or repeal and the actions of the Trump Administration in relation to the ACA could have on our business. It is possible that amendment or repeal initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated

revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates. While the timing and scope of any potential future legislation to amend or repeal ACA provisions is highly uncertain in many respects, including the possibility that any such amendment or repeal is brought about by a court ruling rather than legislative action, it is also possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be amended or repealed.

The costs of prescription pharmaceuticals in the United States has also been the subject of considerable discussion in the United States, and members of Congress and the Trump Administration have stated that they will address such costs through new legislative and administrative measures. In May 2018, the Trump Administration announced a plan that would include several initiatives designed to lower drug prices and additional similar proposals from HHS and CMS have followed. In September 2019, members of both houses of Congress unveiled separate bills aimed at controlling drug pricing. At the state level, individual states are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing and to increase the transparency of drug pricing. Additionally, third party payors, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. We expect additional measures addressing pharmaceutical pricing to be proposed and may be adopted in the future, which could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

The pricing of prescription pharmaceuticals is also subject to governmental control outside 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 ability to generate revenues and become profitable could be impaired. In the European Union, similar political, economic and regulatory developments as those in the United States may affect our ability to profitably commercialize our products, if approved.

Finally, legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be 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 commercialization of our product candidates, if any, may be.

We are subject to U.S. and foreign anti-corruption and anti-money laundering laws with respect to our operations and non-compliance with such laws can subject us to criminal and/or civil liability and harm our business.

We are subject to the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. International Travel Act of 1961, the USA PATRIOT Act, and possibly other state and national anti-bribery and anti-money laundering laws in countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, third-party intermediaries, joint venture partners and collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. We may have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. In addition, we may engage third party intermediaries to promote our clinical research activities abroad and/or to obtain necessary permits, licenses, and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of these third-party intermediaries, our employees, representatives, contractors, partners, and agents, even if we do not explicitly authorize or have actual knowledge of such activities.

Noncompliance with anti-corruption and anti-money laundering laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension and/or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage, and other collateral consequences. If any subpoenas, investigations, or other enforcement actions are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management’s attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause us to appoint an independent compliance monitor which can result in added costs and administrative burdens.

If we or our third-party manufacturers fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We and our third-party manufacturers are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and produce hazardous waste products. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources and any coverage provided by our insurance. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Further, with respect to the operations of our third-party contract manufacturers, it is possible that if they fail to operate in compliance with applicable environmental, health and safety laws and regulations or properly dispose of wastes associated with our product candidates or products, we could be held liable for any resulting damages, suffer reputational harm or experience a disruption in the manufacture and supply of our product candidates or products.

Risks Related to Employee Matters and Managing Our Operations

We are a development-stage company with a limited number of employees to oversee our research and development programs and general and administrative functions. We may experience difficulties in recruiting necessary personnel, especially in building our gene therapy capabilities, and in retaining key employees.

We are a development-stage company with a total of 34 full-time employees as of October 30, 2019. These employees support key areas of our business and operations, including clinical operations, regulatory affairs, drug safety, data management, medical affairs, outsourced manufacturing and supply chain management, analytical development and quality assurance, as well as all of our general and administrative functions and public company infrastructure.

We remain highly dependent on David R. Guyer, M.D., our executive chairman, and Glenn P. Sblendorio, our chief executive officer and president, as well as the other principal members of our management, scientific and clinical teams. We do not maintain "key person" insurance for any of our executives or other employees. Although we have entered into letter agreements with our executive officers, each of them and our non-executive employees may terminate their employment with us at any time. As a result, key employees whom we expect to retain to assist with the growth of our business may choose not to remain employees. Additionally, because of our size, we have only a small number of employees supporting some of the key areas of our business and operations. If any of those employees were to leave our company, the loss of their services could seriously disrupt our ability to carry on our operations as planned and seriously harm our ability to successfully implement our business plan.

Furthermore, replacing any of our executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain marketing approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms, if at all, given the competition among numerous pharmaceutical and biotechnology companies for similar personnel, including, in particular, personnel with gene therapy experience. If we choose to conduct additional internal development of Zimura, we expect we will need to hire additional clinical operations and other necessary personnel from this limited pool. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions.

In addition to our employees, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development, pipeline expansion and commercialization strategies. 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. Many consultants and advisors, especially those with gene therapy experience, are high demand and we may not be able to obtain or retain their services for any number of reasons, which could limit our ability to pursue our strategy.

If we fail to establish and maintain effective internal control over financial reporting, our ability to accurately report our financial results could be adversely affected.

A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the company's annual or interim financial statements would not be prevented or detected on a timely basis. If any material weakness in our internal control over financial reporting is discovered or occurs in the future, our financial statements may contain material misstatements and we could be required to restate our financial results. As previously disclosed in July 2015, our management concluded that we experienced a material weakness in internal controls related to technical accounting expertise over the accounting for deferred tax assets and income tax accounting in general during certain prior financial reporting periods. The deficiency in the application of our controls relating to technical accounting expertise over the accounting for deferred tax assets and income tax accounting in general resulted in the audit committee of our board of directors concluding that the relevant financial statements should not be relied upon, and our subsequent restatement of the relevant financial statements.

During the year ended December 31, 2015, we took the following steps to remediate the identified material weakness: we added staffing within our finance department and engaged a nationally recognized accounting firm, in each case, with technical expertise in the area of tax accounting and financial reporting. Our management concluded that the identified material weakness in internal control over financial reporting was fully remediated as of December 31, 2015. Although we have remediated this deficiency in internal control over financial reporting, we cannot be certain that the remedial measures that we took in the past or other measures we take in the future, especially in light of our decreased size as a result of the implementation of our reduction in personnel during the year ended on December 31, 2017, and the associated decrease in staffing in our accounting and finance areas, will ensure that we maintain adequate controls over our financial reporting going forward and, accordingly, additional material weaknesses could occur or be identified. Any additional material weaknesses or combination of deficiencies could materially and adversely affect our ability to provide timely and accurate financial information, and any future deficiencies may impact investors' confidence in our internal controls and our company, which could cause our stock price to decline.

Risks Related to Our Common Stock

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove members of our board of directors and management.

Provisions in our certificate of incorporation and our by-laws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, 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. Among other things, these provisions:

- provide for a classified board of directors such that only one of three classes of directors is elected each year;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- provide for advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require 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 certain provisions of our certificate of incorporation or by-laws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for stockholders.

Our stock price may be volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. The stock market in general, and the market for smaller pharmaceutical and biotechnology companies in particular, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our stockholders may not be able to sell their shares of common stock at or above the price at which they purchased their shares. The market price for our common stock may be influenced by many factors, including:

- results of research, preclinical development activities and clinical trials for our product candidates and the timing of the receipt of such results;
- the success of products or technologies that compete with our product candidates, including results of clinical trials of product candidates of our competitors;
- the results of our efforts to in-license or acquire the rights to other product candidates and technologies for the treatment of retinal diseases;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or development programs;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions;
- political, regulatory or legal developments in the United States and other countries; and
- the other factors described in this “Risk Factors” section.

For example, following our announcement of initial, top-line results from our OPH2007 Phase 2a clinical trial for Zimura in combination with the anti-VEGF agent Lucentis for the treatment of wet AMD, the closing price of our common stock declined from $2.22 on November 9, 2018 to $1.92 on November 14, 2018 and declined further in the eleven months thereafter. Following periods of volatility in the market price of a company’s stock, securities class-action litigation has often been instituted against that company. For example, we and certain of our current and former executive officers have been named as defendants in a purported class action lawsuit and a related shareholder derivative action following our announcement in December 2016 of the initial, top-line results from the first two of our Phase 3 Fovista trials for the treatment of wet AMD. See Part II, Item 1 of this Quarterly Report on Form 10-Q and in this "Risk Factors" section, “*Risks Related to Our Business Plan, Financial Position and Need for Additional Capital—We and certain of our current and former executive officers have been named as defendants in lawsuits that could result in substantial costs and divert management’s attention*.” These proceedings and other similar litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert management’s attention and resources, which could seriously harm our business.

If a significant portion of our total outstanding shares are sold into the market, the market price of our common stock could drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. For example, we issued 5,174,727 shares of our common stock to the former equityholders of Inception 4 as upfront consideration for our acquisition of Inception 4. These shares were subject to lock-up restrictions, which expired at

the end of April 2019 with respect to 50% of such shares and at the end of October 2019 with respect to the remaining 50% of such shares, following which such shares may be freely sold and traded pursuant to a registration statement on Form S-3 (File No. 333-229978) that was declared effective by the Securities and Exchange Commission on April 25, 2019. If the holders of these shares sell, or the market perceives that these holders will sell, the shares currently held by them, the price of our common stock may decline.

Moreover, we have filed, and expect to continue to file, registration statements on Form S-8 registering all shares of common stock that we may issue under our equity compensation plans, including our recently adopted 2019 Inducement Stock Incentive Plan. Once registered on Form S-8, shares underlying these equity awards can be freely sold in the public market upon issuance, subject to volume, notice and manner of sale limitations applicable to affiliates.

We incur increased costs as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives and corporate governance practices.

As a public company, we incur and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time-consuming and costly.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish with our periodic Exchange Act reports a report by our management on our internal control over financial reporting. We are also required to include with our annual report an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404, we must 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 and engage outside consultants 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. There is a risk that our internal control over financial reporting may, in the future, be found to be ineffective under Section 404. Our identification of one or more material weaknesses could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, will be our stockholders' sole source of gain.

We have never declared or paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth of our business. In addition, the terms of any future debt agreements that we enter into may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds.

Recent Sales of Unregistered Securities

On July 22, 2019, we issued to the University of Massachusetts 75,000 shares of our common stock, par value $0.001 per share, as upfront consideration for the exclusive license agreement for our miniCEP290 program. Based on and relying on certain representations made by the University of Massachusetts, we issued these shares pursuant to an exemption from registration afforded by Section 4(a)(2) of the Securities Act of 1933, as amended. We did not sell any other unregistered equity securities during the period covered by this Quarterly Report on Form 10-Q.

Purchase of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Quarterly Report on Form 10-Q.

Item 5. Other Information

None.

Item 6. Exhibits and Financial Statement Schedules

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.

(2) Financial Statement Schedules

No financial statement schedules have been filed as part of this Quarterly Report on Form 10-Q because they are not applicable, not required or because the information is otherwise included in our financial statements or notes thereto.

(3) Exhibits

Exhibit Number	Description of Exhibit
3.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.3 to Amendment No. 2 of the Registrant's Registration Statement on Form S-1 (File No. 333-190643) filed with the Securities and Exchange Commission on September 9, 2013)
3.2	Certificate of Amendment to Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 of the Registrant's Current Report on Form 8-K filed with the Securities and Exchange Commission on April 16, 2019)
3.3	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.4 to Amendment No. 2 of the Registrant's Registration Statement on Form S-1 (File No. 333-190643) filed with the Securities and Exchange Commission on September 9, 2013)
10.1 †	Exclusive License Agreement, by and between the University of Massachusetts and Registrant, dated July 22, 2019
10.2	Amendment No. 1 to Master Sponsored Research Agreement, by and between The Trustees of the University of Pennsylvania and Registrant, dated October 1, 2019
10.3	Amendment No. 1 to Master Sponsored Research Agreement, by and between The Trustees of the University of Pennsylvania and Registrant, dated October 1, 2019
10.4	2019 Inducement Stock Incentive Plan of the Registrant (incorporated by reference to Exhibit 99.1 to the Registrant's Registration Statement on Form S-8 (File No. 333-234404) filed with the Securities and Exchange Commission on October 31, 2019)
10.5	Form of Restricted Stock Unit Agreement under the 2019 Inducement Stock Incentive Plan of the Registrant (incorporated by reference to Exhibit 99.2 to the Registrant's Registration Statement on Form S-8 (File No. 333-234404) filed with the Securities and Exchange Commission on October 31, 2019)
10.6	Form of Nonstatutory Stock Option Agreement under the 2019 Inducement Stock Incentive Plan of the Registrant (incorporated by reference to Exhibit 99.3 to the Registrant's Registration Statement on Form S-8 (File No. 333-234404) filed with the Securities and Exchange Commission on October 31, 2019)
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended
32.1	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS*	XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Calculation Linkbase Document
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	XBRL Taxonomy Label Linkbase Document
101.PRE*	XBRL Taxonomy Presentation Linkbase Document

***** Submitted electronically herewith.

† Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

Attached as Exhibit 101 to this report are the following formatted in XBRL (Extensible Business Reporting Language): (i) Consolidated Balance Sheets at September 30, 2019 (unaudited) and December 31, 2018, (ii) Consolidated Statements of Operations and Comprehensive Loss (unaudited) for the three and nine month periods ended September 30, 2019 and 2018, (iii) Consolidated Statements of Stockholders' Equity (unaudited) for the three and nine month periods ended September 30,

2019 and 2018, (iv) Consolidated Statements of Cash Flows (unaudited) for the nine month periods ended September 30, 2019 and 2018 and (v) Notes to Financial Statements (unaudited).

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.

IVERIC bio, Inc.

Date: November 12, 2019

By: /s/ David F. Carroll

David F. Carroll
Chief Financial Officer
(Principal Financial and Accounting Officer)

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) would likely cause competitive harm to the Company, if publicly disclosed. Double asterisks denote omissions.

EXCLUSIVE LICENSE AGREEMENT

This Agreement, effective as of **July 22, 2019** (the "Effective Date"), is between the **University of Massachusetts** ("University"), a not-for-profit, public institution of higher education of the Commonwealth of Massachusetts, established by Chapter 75 of the Massachusetts General Laws, as represented by and solely on behalf of its Medical School (Worcester campus) and **IVERIC bio, Inc.** ("Company"), a Delaware corporation.

RECITALS

WHEREAS, University owns certain intellectual property rights which relate to gene therapies of the *CEP290* gene for the treatment of Leber Congenital Amaurosis (LCA) type 10, as described in University's docket UMMS 17-04, entitled "Novel Gene Therapeutic Molecules for CEP290-LCA" and associated patent applications, as further described in **Exhibit A**;

WHEREAS, Company is engaged in business relating to the development and commercialization of products that use or incorporate University's intellectual property rights and has the capability of developing commercial applications of the intellectual property;

WHEREAS, Company desires to obtain an exclusive license to University's intellectual property rights, and University is willing to grant an exclusive license to its intellectual property rights under the following conditions so that these intellectual property rights may be developed to their fullest and the benefits enjoyed by the general public; and

WHEREAS, the license that is granted in this Agreement promotes the development of publicly funded intellectual property to practical application for the public good.

THEREFORE, University and Company agree as follows:

1. Definitions.

1.1. "Affiliate" means an entity that controls, is controlled by, or is under common control with a party to this Agreement. The term "control" as used in the preceding sentence means possession of the power to direct or call for the direction of the management and policies of an entity, whether through ownership of a majority of the outstanding voting securities, by contract, or otherwise.

1.2. "Biological Materials" means tangible biological materials that are necessary for the effective exercise of the Patent Rights, which materials are described on **Exhibit B**, as well as tangible materials that are produced by or on behalf of Company, its Affiliates or Sublicensees through use of the original materials, including, for example, any progeny derived from a cell line, monoclonal antibodies produced by hybridoma cells, DNA or RNA replicated from isolated DNA or RNA, recombinant proteins produced through use of isolated DNA or RNA, and substances purified from a source material included in the original materials (such as, recombinant proteins isolated from a cell extract or supernatant by non-proprietary affinity purification methods).

1.3. "Confidential Information" means any confidential or proprietary information furnished by one party (the "Disclosing Party") to the other party (the "Receiving Party") in connection with this Agreement that is specifically designated as confidential, as further described in Article 7.

1.4. "FDA" means the U.S. Food and Drug Administration or any successor agency.

1.5. “Field” means the prevention, treatment, cure or control of any human indication, disease, disorder or condition relating to the *CEP290* gene. Any commercial sale of research reagents covered by the Patent Rights is specifically excluded from the Field.

1.6. “IND” means an Investigational New Drug Application, as defined in the U.S. Federal Food, Drug and Cosmetic Act.

1.7. “Licensed Product” means any product that cannot be developed, manufactured, used, or sold without infringing one or more Valid Claims.

1.8. "Licensed Know-How" means know-how owned or controlled by University as of the Effective Date, that (i) is not generally known, and (ii) is necessary or reasonably useful to research, develop, manufacture, use and/or sell the Licensed Product and/or to practice the Patent Rights or the Biological Materials.

1.9. “Net Sales” means, the gross amount billed or invoiced on sales of Licensed Products by Company, its Affiliates and Sublicensees, less deductions actually taken or applied, as determined in accordance with, and as permitted by, U.S. generally accepted accounting principles as consistently applied across Company’s, its Affiliates’ and Sublicensees’ (as applicable) pharmaceutical products generally, including the following:

(a) customary trade quantity, or cash discounts to non-affiliated brokers or agents to the extent actually allowed and taken;

(b) amounts repaid or credited by reason of rejection or return or because of chargebacks, rebates or retroactive price reductions;

(c) to the extent separately stated on purchase orders, invoices, or other documents of sale, any taxes or other governmental charges levied on the production, sale, transportation, delivery, or use of a Licensed Product which is paid by or on behalf of Company, its Affiliates or Sublicensees;

and (d) outbound transportation costs prepaid or allowed and costs of insurance in transit.

In any transfers of Licensed Products between any of Company and its Affiliates and Sublicensees, Net Sales are calculated based on the final sale of the Licensed Product to an independent third party. If Company or an Affiliate or Sublicensee receives non-monetary consideration for any Licensed Products, Net Sales are calculated based on the fair market value of that consideration. If Company or any of its Affiliates or Sublicensees uses or disposes of a Licensed Product in the provision of a commercial service, the Licensed Product is sold and the Net Sales are calculated based on the sales price of the Licensed Product billed or invoiced by such entity to an independent third party during the same Royalty Period or, in the absence of sales, on the fair market value of the Licensed Product as determined by Company and University in good faith.

1.10. “Patent Rights” means the United States and PCT patent applications listed or referred to in Exhibit A and patent applications covering invention disclosures listed or referred to in Exhibit A, if any, and any divisional, continuation, or continuation-in-part of those patent applications to the extent the claims are directed to subject matter specifically described therein as well as any patents issued on these patent applications or resulting from post-grant proceedings and any reissues, substitutions, reexaminations or extensions of the patents, and any foreign counterparts to any of the foregoing.

1.11. “Royalty Period” means the partial calendar quarter commencing on the date on which the first Licensed Product is sold and every complete or partial calendar quarter thereafter during which either (a) this Agreement remains in effect or (b) Company has the right to complete and sell work-in-progress and inventory of Licensed Products pursuant to Section 8.5.

1.12. "Sublicense Agreement" means any agreement in which Company grants, or promises to grant, rights to the Patent Rights, Biological Materials, or Licensed Know-How pursuant to Section 2.2, including by way of example but not limitation, sublicenses, options, rights of first refusal, rights of first negotiation, etc. For the avoidance of doubt, any agreement that confers or promises to confer rights under this Agreement, regardless of its name or title, shall be deemed to be a Sublicense Agreement. For clarity, distribution agreements and manufacturing agreements are considered Sublicense Agreements if the distributor or manufacturer entering into these agreements with the Company makes payments to the Company (other than payments for sales of Licensed Products) for obtaining distribution and manufacturing rights.

1.13. "Sublicense Income" means any payments or other value that Company or any of its Affiliates receives from a Third Party Sublicensee in consideration of the Sublicense Agreement, including without limitation, upfront fees, option fees, license fees, equity, milestone payments, and license maintenance fees, etc., but excluding the following payments: (a) payments made in consideration for the issuance of equity or debt securities of Company at fair market value, (b) payments specifically committed to the further development or manufacture of Licensed Products and (c) royalties. [**].

1.14. "Sublicensee" means any permitted sublicensee of the rights granted to Company under this Agreement, as further described in Section 2.2.

1.15. "Third Party" means any entity or person other than University and its Affiliates, on the one hand, and Company and its Affiliates, on the other hand.

1.16. "Valid Claim" means (a) a claim of an issued and unexpired patent covering the Patent Rights which has not been permanently revoked or held unenforceable or invalid by an un-appealable or un-appealed decision of a court or government agency of competent jurisdiction or (b) a claim of a pending patent application within the Patent Rights that has not been abandoned or finally disallowed without the possibility of appeal or refiling.

2. Grant of Rights

2.1. License Grant. University hereby grants to Company an exclusive, worldwide, royalty-bearing license in the Patent Rights and the Biological Materials and a non-exclusive license to the Licensed Know-How to make, have made, use, offer to sell, sell, have sold and import Licensed Products in the Field, including research for development of Licensed Products.

2.2. Sublicenses. Company may grant sublicenses of its rights under Section 2.1. All Sublicense Agreements executed by Company pursuant to this Section 2.2 shall expressly bind the Sublicensee to the terms of this Agreement. Company shall promptly furnish University with a fully executed, un-redacted copy of any Sublicense Agreement.

2.3. Retained Rights.

(a) University. University retains the right to use the Patent Rights for academic research, teaching, and non-commercial patient care, without payment of compensation to Company. University may license its retained rights under this Subsection 2.3(a) to non-commercial research collaborators of University faculty members, post-doctoral fellows, and students.

(b) Federal Government. University informs Company and Company understands that the federal government has funded certain inventions claimed in the Patent Rights and therefore this Agreement and the grant of any rights in Patent Rights are subject to the federal law set forth in 35 U.S.C. §§ 201-211 and the regulations promulgated thereunder, as amended, or any successor statutes or regulations. Company acknowledges that these statutes and regulations reserve to the federal government a royalty-free, non-exclusive, non-transferrable license to practice any government-funded invention claimed in the Patent Rights. If any term of this Agreement

fails to conform to those laws and regulations, the relevant term is invalid, and the parties shall modify the term pursuant to Section 10.11.

3. Company Obligations Relating to Development and Commercialization.

3.1. Diligence Requirements. Company shall use diligent efforts or cause its Affiliates and Sublicensees to use diligent efforts to develop Licensed Products and to introduce Licensed Products into the commercial market. Following marketing approval, Company or its Affiliates or Sublicensees shall make Licensed Products reasonably available to the public. Specifically, Company shall fulfill the following obligations:

(a) Financing the Company. University acknowledges that Company is a public company. Company shall maintain adequate financial resources to fulfill its diligence obligations under this Agreement.

(b) Development of Licensed Products.

(i) On or before execution of this Agreement, Company shall furnish University with a written research and development plan under which Company intends as of the Effective Date to develop Licensed Products.

(ii) Within [**] after the start of each calendar year, beginning with calendar year 2020, Company shall furnish University with a written report on progress during the prior year to develop and commercialize Licensed Products, including without limitation research and development, efforts to obtain regulatory approval, marketing, and sales figures. The Company shall also include in the report a discussion of its intended development and commercialization efforts for the current year.

(iii) Within [**] after the Effective Date, Company, its Affiliate or Sublicensee shall have [**].

(iv) Within [**] after the Effective Date, Company, its Affiliate or Sublicensee shall have [**].

(v) Within [**] after the Effective Date, Company, its Affiliate or Sublicensee shall have [**].

(vi) Within [**] after the Effective Date, Company, its Affiliate or Sublicensee shall have [**].

(vii) Within [**] after [**], Company, its Affiliate or Sublicensee shall [**].

3.2. Extensions of Diligence Obligations. If the Company requires an extension of any milestones or due dates set forth in Section 3.1(b)(iii)-(vii), Company shall inform University of such extension in writing at least [**] prior to the required due date, fully describing Company's efforts to achieve the milestone to date, establishing the new due date, and describing Company's plan to meet such new due date. Later-in-time milestone due dates shall automatically be deemed to have been extended by the same amount of time. However, if University reasonably objects to such extension within [**] after receipt of Company's extension notice, the terms of such extension (including whether to grant such extension) shall be negotiated by the parties in good faith, unless Company sends to University documentation demonstrating that Company, its Affiliates and its Sublicensees have collectively spent the below amounts in respect of the Licensed Product whose milestones Company is seeking to extend, in which case University's objection as to whether to grant an extension shall be deemed to have been overcome, and the parties shall agree on reasonable extension dates; however, Company may only use such justification for an extension [**] per milestone.

Timing of Extension Request	Amount Spent by Company, its Affiliates and Sublicensees for the relevant Licensed Product in the [**] Prior to Extension Request
[**]	[**]
[**]	[**]
[**]	[**]

If at any time University reasonably determines that Company has not fulfilled its obligations under Subsection 3.1(b), University shall furnish Company with written notice of the determination. Within [**] after receipt of the notice if Company is not entitled to an extension, Company shall either (a) fulfill the relevant obligation or (b) negotiate with University a mutually acceptable schedule of revised diligence obligations, failing which University may, immediately upon written notice to Company, terminate this Agreement or convert the exclusive license into a non-exclusive license.

3.3. Indemnification.

(a) Indemnity. Company shall indemnify, defend, and hold harmless University and its trustees, officers, faculty, students, employees, and agents and their respective successors, heirs and assigns (the "Indemnitees"), against any liability, damage, loss, or expense (including reasonable attorneys' fees and expenses of litigation) incurred by or imposed upon any of the Indemnitees in connection with any Third Party claims, suits, actions, demands or judgments arising out of any theory of liability (including without limitation actions in the form of tort, warranty, or strict liability and regardless of whether the action has any factual basis) concerning any product, process, or service that is made, used, or sold pursuant to any right or license granted under this Agreement. However, indemnification does not apply to any liability, damage, loss, or expense to the extent directly attributable to (i) the gross negligence or intentional misconduct of the Indemnitees or (ii) the settlement of a claim, suit, action, or demand by Indemnitees without the prior written approval of Company.

(b) Procedures. The Indemnitees agree to provide Company with prompt written notice of any claim, suit, action, demand, or judgment for which indemnification is sought under this Agreement. Company agrees, at its own expense, to provide attorneys reasonably acceptable to University to defend against any such claim. The Indemnitees shall cooperate fully with Company in the defense and will permit Company to conduct and control the defense and the disposition of the claim, suit, or action (including all decisions relative to litigation, appeal, and settlement). However, any Indemnitee may retain its own counsel, at the expense of Company, if representation of the Indemnitee by the counsel retained by Company would be inappropriate because of actual or potential conflicts in the interests of the Indemnitee and any other party represented by that counsel. Company agrees to keep University informed of the progress in the defense and disposition of the claim and to consult with University regarding any proposed settlement.

(c) Insurance. Company shall maintain insurance or self-insurance that is reasonably adequate to fulfill any potential obligation to the Indemnitees, but not less than [**] dollars ($[**]) for injuries to any one person arising out of a single occurrence and [**] dollars ($[**]) for injuries to all persons arising out of a single occurrence. Company shall provide University with written evidence of insurance or self-insurance; provided that Company shall increase the coverage for injuries to all persons to at least [**] dollars ($[**]), prior to commencing any clinical trials with a Licensed Product. Company shall purchase insurance for clinical trials covering the relevant geographies to take effect no later than the start of dosing in human patients. Company shall continue to maintain the insurance or self-insurance after the expiration or termination of this Agreement while Company, its Affiliate or Sublicensee continues to make, use, or sell a Licensed Product and thereafter for [**]; provided, that, if pursuant to Section 8.5, Company elects for any Sublicensee to survive as a direct licensee of University following early termination of this Agreement, such Sublicensee shall continue to be bound by the insurance obligations of this Section but only as an independent licensee of University and no longer as a Sublicensee of Company.

3.4. Use of University Name. Except as permitted by Section 7.2, Company and its Affiliates and Sublicensees may not use the name "University of Massachusetts" or any variation of that name in connection with the marketing or sale of any Licensed Products.

3.5. Marking of Licensed Products. To the extent commercially feasible and consistent with prevailing business practices, Company shall mark and shall cause its Affiliates and Sublicensees to mark all Licensed Products that are manufactured or sold under this Agreement with the number of each issued patent under the Patent Rights that applies to a Licensed Product.

3.6. Compliance with Law. Company shall comply with, and shall ensure that its Affiliates and Sublicensees comply with, all applicable local, state, federal, and international laws and regulations relating to the development, manufacture, use, and sale of Licensed Products. Company expressly agrees to comply with the following:

(a) Company or its Affiliates or Sublicensees shall obtain all necessary approvals from the FDA and any similar foreign governmental authorities in which Company or Affiliate or Sublicensee intends to make, use, or sell Licensed Products.

(b) Company and its Affiliates and Sublicensees shall comply with all United States laws and regulations controlling the export of commodities and technical data, including without limitation all Export Administration Regulations of the United States Department of Commerce. Among other things, these laws and regulations prohibit or require a license for the export of certain types of commodities and technical data to specified countries and foreign nationals. Company hereby gives written assurance that it will comply with and will cause its Affiliates and Sublicensees to comply with all United States export control laws and regulations, that it bears sole responsibility for any violation of those laws and regulations by itself or its Affiliates or Sublicensees, and that it will indemnify, defend, and hold University harmless (in accordance with Section 3.3) for the consequences of any violation.

(c) If any invention claimed in the Patent Rights has been funded by the United States government, and only to the extent required by applicable laws and regulations, Company agrees that any Licensed Products used or sold in the United States will be manufactured substantially in the United States or its territories. Current law provides that if domestic manufacture is not commercially feasible under the circumstances, University may seek a waiver of this requirement from the relevant federal agency on behalf of Company.

4. Consideration for Grant of Rights.

4.1. License Fee. In partial consideration of the rights granted Company under this Agreement, Company shall pay to University on the Effective Date a license fee of four hundred thousand Dollars ($400,000). This license fee payment is nonrefundable and not creditable against any other payments due to University under this Agreement.

4.2. Upfront Shares. In partial consideration of the rights granted Company under this Agreement, and on the basis of the representations, warranties and acknowledgments described in Section 10.1.2 of this Agreement, Company shall issue to University, promptly after the Effective Date, 75,000 shares of the Company's common stock, par value $0.001 per share ("Company Common Stock") (such shares, the "Upfront Shares").

4.3. License Maintenance Fee. During the term of this Agreement, on each anniversary of the Effective Date until the expiration of the Royalty Term, commencing on July 22, 2020, Company shall pay to University [**] Dollars ($[**]). This annual license maintenance fee is nonrefundable and is not creditable against any other payments due to University under this Agreement.

4.4. Milestone Payments. Company shall pay University the following one-time (for all Licensed Products) milestone payments within [**] after the first occurrence of the applicable event for any Licensed Product:

	Clinical or Regulatory Milestone	Payment
A	[**]	75,000 shares of Company Common Stock
B	[**]	[**]
C	[**]	[**]
D	[**]	[**]
E	[**]	[**]
F	[**]	[**]
G	[**]	[**]

These milestone payments are nonrefundable and are not creditable against any other payments due to University under this Agreement. Company shall make all milestone payments that are achieved, in addition to any of milestones [**] if such milestone event has not been achieved prior to the achievement of a later milestone (and, for clarity, there shall be [**] with respect to milestones [**]). For example, if Company [**], the milestone payments for [**] are due upon achievement of the [**] milestone event. Also, as a further example, if Company [**], then upon [**] in [**] above, [**] milestone payments are due.

Additionally, with respect to the milestone set forth in A above, (a) the number of shares of Company Common Stock that will be issuable or issued upon the achievement of such milestone (such shares, if any, the "Milestone Shares" and, together with the Upfront Shares, the "Shares"), will be adjusted equitably by the Company in the manner determined by its board of directors in the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, or other similar change in the capitalization of or event affecting the Company before issuance of such shares, including any distribution to holders of Company Common Stock other than ordinary cash dividends, and (b) in the event of a Reorganization Event occurring before achievement of the milestone and in which holders of Company Common Stock receive cash, securities or other property upon consummation of the Reorganization Event, the milestone payment obligation shall remain outstanding and upon achievement of the milestone, University shall receive a milestone payment in the same type as (e.g., cash, securities, or other property) and equal in amount to what such holders of Company Common Stock holding 75,000 shares of Company Common Stock immediately prior to consummation of such Reorganization Event would have received (and if holders of Company Common Stock were offered a choice of consideration or provided different kinds of consideration, then the type of consideration chosen by or given to the holders of a majority of the outstanding shares of Company Common Stock), less any applicable tax withholdings. For purposes of the foregoing, a "Reorganization Event" is: (i) any merger or consolidation of the Company with or into another entity as a result of which all Company Common Stock is converted into or exchanged for the right to receive cash, securities or other property or is cancelled, (ii) any transfer or disposition of all Company Common Stock for cash, securities or other property pursuant to a share exchange or other transaction, or (iii) any liquidation or dissolution of the Company. In connection with and as a condition to any payment of milestone A above, University agrees to deliver a certificate to Company (or its successor) substantially in the form of **Exhibit C** hereto. In the event of any payment of milestone A above made prior to any occurrence of a Reorganization Event, Company agrees to deliver a certificate to University substantially in the form of **Exhibit D** hereto. In the event of any payment of milestone A above made after any occurrence of a Reorganization Event, Company or its successor or acquirer agrees to deliver a certificate to University in which Company or such successor or acquirer certifies to the accuracy of representations and warranties set forth in Section 10.1.1 as modified appropriately for Company or such successor or acquirer and for the type of consideration to be paid for milestone A.

Commercial Milestone	Payment
First instance of calendar year worldwide Net Sales of $[**]	[**]
First instance of calendar year worldwide Net Sales of $[**]	[**]
First instance of calendar year worldwide Net Sales of $[**]	[**]
First instance of calendar year worldwide Net Sales of $[**]	[**]

By way of example, if Company achieves $[**] of calendar year worldwide Net Sales of a Licensed Product in Year 1; $[**] of calendar year worldwide Net Sales of a Licensed Product in Year 2; and $[**] of calendar year worldwide Net Sales of a Licensed Product in Year 3, then Licensee will owe [**] commercial milestones for Year 1; $[**] in commercial milestones for Year 2 and $[**] in commercial milestones for Year 3.

4.5. Royalties. Company shall pay to University a royalty of [**] percent ([**]%) of Net Sales of each Licensed Product in each country where a Valid Claim covers the sale of such Licensed Product in such country. These royalties are payable, on a Licensed Product-by-Licensed Product and country-by-country basis, for the longer of: (i) so long there remains any Valid Claim covering the sale of such Licensed Product in such country; or (ii) ten (10) years from the first commercial sale of such Licensed Product in such country (the "Royalty Term"); provided, however that any royalties that are due under this Agreement during the Royalty Term but after the expiration of the Patent Rights shall be a deferred royalty for the period from the Effective Date until start of the Royalty Period during which no royalty shall have otherwise been due.

4.6. Minimum Royalty. During the term of this Agreement, within [**] after the beginning of each calendar year following receipt of FDA marketing approval for any Licensed Product and until the expiration of the Royalty Term, Company shall pay to University a minimum royalty of [**] Dollars ($[**]). Company may credit the minimum royalty paid under this Section 4.6 against actual royalties due and payable for the same calendar year. Waiver of any minimum royalty payment by University is not a waiver of any subsequent minimum royalty payment. If Company fails to make any required minimum royalty payment within the [**] period, that failure is a material breach of its obligations under this Agreement, and University may terminate this Agreement in accordance with Section 8.3 (subject to Company's cure right set forth therein).

4.7. Sublicense Income. Company shall pay University the following percentages of all Sublicense Income:

(a) [**] percent ([**]%) for Sublicense Agreements that are executed by Company from the Effective Date and prior to [**];

(b) [**] percent ([**]%) for Sublicense Agreements that are executed by Company from and after [**];

(c) [**] percent ([**]%) for Sublicense Agreements that are executed by Company from and after [**]; and

(d) [**] percent ([**]%) for Sublicense Agreements that are executed by Company from and after [**].

Sublicense Income is due within [**] after Company receives the relevant payment from the Third Party Sublicensee.

4.8. Priority Review Voucher. If Company is awarded a priority review voucher by the FDA or other U.S. governmental agency based on a regulatory approval of a Licensed Product (a "Voucher") and Company or any of its Affiliates realizes any Net Profit (as defined below) from the sale to a Third Party of any such Voucher,

then Company shall pay to University an amount equal to [**] percent ([**]%) of all such Net Profit. If such a Voucher is not sold by Company or any of its Affiliates, but instead is used by Company or any of its Affiliates for the benefit of any product outside the Agreement that is not a Licensed Product, then, (a) at the time of receipt of marketing approval from the FDA of the product to which such Voucher was applied, Company shall pay to University an amount equal to [**] percent ([**]%) of the fair market value of such Voucher, and (b) after the first instance of the Company (and its Affiliates and (sub)licensees) achieving worldwide net sales for such approved product of $[**] or greater in any calendar year, Company shall pay to University an amount equal to [**] percent ([**]%) of the fair market value of such Voucher. In each such case, the fair market value shall be agreed by the parties based on recent sales of comparable vouchers, as of the occurrence of the event in (a). As used herein, the term "Net Profits" shall mean (i) the aggregate sale price received by Company and its Affiliates from a sale of the Voucher to a Third Party, including all monies, cash equivalents and the fair market value of other consideration, less (ii) all reasonable out-of-pocket expenses incurred by Company and its Affiliates directly related to marketing and selling the Voucher, including legal fees, financial advisor fees and third party broker or finder fees paid to Third Parties.

5. Royalty Reports; Payments; Records.

5.1. First Sale. Company shall report to University the date of first commercial sale of each Licensed Product within [**] after occurrence in each country.

5.2. Reports and Payments.

(a) Within [**] after the conclusion of each Royalty Period, Company shall deliver to University a report containing the following information:

(i) the number of Licensed Products sold to independent third parties in each country and the number of Licensed Products used by Company, its Affiliates and Sublicensees in the provision of services in each country;

(ii) the gross sales price for each Licensed Product by Company, its Affiliates and Sublicensees during the applicable Royalty Period in each country;

(iii) calculation of Net Sales for the applicable Royalty Period in each country, including a listing of applicable deductions;

(iv) total royalty payable on Net Sales in United States dollars, together with the exchange rates used for conversion; and

(v) Sublicense Income due to University for the applicable Royalty Period from each Sublicensee.

(b) Concurrent with this report, Company shall remit to University any payment due for the applicable Royalty Period. If no royalties are due to University for any Royalty Period, the report shall so state.

5.3. Payments in United States Dollars. Company shall make all payments in United States dollars. Company shall convert foreign currency to United States dollars at the conversion rate existing in the United States (as reported in the *Wall Street Journal*) on the last working day of the applicable Royalty Period. Company may not deduct exchange, collection, or other charges.

5.4. Payments in Other Currencies. If by law, regulation, or fiscal policy of a particular country, conversion into United States dollars or transfer of funds of a convertible currency to the United States is restricted or forbidden, Company shall give University prompt written notice of the restriction within the [**] payment deadline described in Section 5.2. Company shall pay any amounts due University through whatever lawful methods University reasonably designates. However, if University fails to designate a payment method within [**]

after University is notified of the restriction, Company may deposit payment in local currency to the credit of University in a recognized banking institution selected by Company and identified by written notice to University, and that deposit fulfills all obligations of Company to University with respect to that payment.

5.5. Records. Company shall maintain and shall cause its Affiliates and Sublicensees to maintain complete and accurate records of Licensed Products that are made, used, or sold under this Agreement and any amounts payable to University in relation to Licensed Products with sufficient information to permit University to confirm the accuracy of any reports delivered to University under Section 5.2. The relevant party shall retain records relating to a given Royalty Period for at least [**] after the conclusion of that Royalty Period, during which time University may, at its expense, cause its internal accountants or an independent, certified public accountant to inspect records during normal business hours for the sole purpose of verifying any reports and payments delivered under this Agreement. The accountant may not disclose to University any information other than information relating to accuracy of reports and payments delivered under this Agreement. The parties shall reconcile any underpayment or overpayment within [**] after the accountant delivers the results of the audit. If any audit performed under this Section 5.5 reveals an underpayment in excess of [**] percent ([**]%) in any Royalty Period, Company shall bear the full cost of the audit. University may exercise its rights under this Section 5.5 only [**] and only with reasonable prior notice to Company.

5.6. Late Payments. Any payments by Company that are not paid on or before the date payments are due under this Agreement, unless such payments are being disputed in good faith, shall bear interest at [**]% per month (or if such rate exceeds the maximum rate permitted by law, then at the maximum rate permitted by law), calculated on the number of days that payment is delinquent.

5.7. Method of Payment. All payments under this Agreement should be made to the “University of Massachusetts” and sent to the address identified below in Section 10.10 or as otherwise instructed by the University from time to time. Each payment should reference this Agreement and identify the obligation under this Agreement that the payment satisfies.

5.8. Withholding and Similar Taxes. Royalty payments and other payments due to University under this Agreement may not be reduced by reason of any withholding or similar taxes applicable to payments to University. Therefore, all amounts owed to University under this Agreement are net amounts and shall be grossed-up to account for any withholding taxes, value-added taxes or other taxes, levies or charges.

6. Patents and Infringement.

6.1. Responsibility for Patent Rights.

(a) University has primary responsibility at the expense of Company for the preparation, filing, prosecution, and maintenance of all Patent Rights, using patent counsel reasonably acceptable to Company. University shall consult with Company as to the strategy for prosecution of the Patent Rights (for example, whether to prosecute certain patents or patent applications, and/or in certain countries) and as to preparation, filing, prosecution, and maintenance of all Patent Rights reasonably prior to any deadline or action with the United States Patent & Trademark Office (USPTO) or any foreign patent office, and shall furnish Company with copies of relevant documents reasonably in advance of consultation. University shall give due consideration to any comments of Company or its patent counsel on strategy for prosecution of the Patent Rights, any patent filings for the Patent Rights and any responses to correspondence from or actions of the USPTO or any foreign patent office relating to the Patent Rights.

(b) If University desires to abandon any patent or patent application within the Patent Rights, University shall provide Company with reasonable prior notice of the intended abandonment, and Company may, at its expense, prepare, file, prosecute, and maintain the relevant Patent Rights.

6.2. Cooperation. Each party shall provide reasonable cooperation in the preparation, filing, prosecution, and maintenance of all Patent Rights. Cooperation includes, without limitation, promptly informing

the other party of matters that may affect the preparation, filing, prosecution, or maintenance of Patent Rights (such as, becoming aware of an additional inventor who is not listed as an inventor in a patent application).

6.3. Payment of Expenses.

(a) Within [**] after University invoices Company, Company shall reimburse University for all previously unreimbursed expenses incurred as of the Effective Date in connection with obtaining the Patent Rights.

(b) Within [**] after University invoices Company, Company shall reimburse University for all patent-related expenses that have not been paid under Subsection 6.3(a) and that are incurred by University pursuant to Section 6.1. Company may elect, upon [**] written notice to University, to cease payment of the expenses associated with obtaining or maintaining patent protection for one or more Patent Rights in one or more countries. If Company elects to cease payment of any patent expenses, Company loses all rights under this Agreement with respect to the particular Patent Rights in those one or more countries.

6.4. Infringement.

(a) Notification of Infringement. Each party agrees to provide written notice to the other party promptly after becoming aware of any infringement of the Patent Rights, including any proceedings instituted by a Third Party seeking a declaratory judgment that any of the Patent Rights are unenforceable or invalid or not infringed by such Third Party, or any post-grant or *inter partes* review proceedings with similar effect.

(b) Company Right to Prosecute. As long as Company remains the exclusive licensee of the Patent Rights in the Field, Company may, under its own control and at its own expense, prosecute any third party infringement of the Patent Rights in the Field or, together with licensees of the Patent Rights in other fields (if any), defend the Patent Rights in any declaratory judgment action brought by a Third Party which alleges invalidity, unenforceability, or non-infringement of the Patent Rights. Prior to commencing any action, Company shall consult with University and shall consider the views of University regarding the advisability of the proposed action and its effect on the public interest. Company may not enter into any settlement, consent judgment, or other voluntary final disposition (each, a "Settlement") of any infringement action under this Subsection 6.4(b), without the prior written consent of University, which consent may not be unreasonably withheld or delayed. Any recovery obtained in an action under this Subsection 6.4(b) shall be distributed as follows: (i) first, each party shall be reimbursed for any expenses incurred in the action; and (ii) second, as to ordinary damages, Company shall receive an amount equal to its lost profits or a reasonable royalty on the infringing sales (whichever measure of damages the court applied), less a reasonable approximation of the royalties that Company would have paid to University if Company had sold the infringing products and services rather than the infringer, which amount the University shall receive, and as to the remainder of ordinary damages, if any, the parties shall share equally, and as to special, treble or punitive damages, the parties shall share equally in any award.

(c) University as Indispensable Party. University shall permit any action under Subsection 6.4(b) to be brought in its name if required by law, provided that Company shall hold University harmless from, and if necessary indemnify University against, any costs, expenses, or liability that University may incur in connection with the action.

(d) University Right to Prosecute. If Company fails to initiate an infringement action within a reasonable time after it first becomes aware of the basis for the action, or to answer a declaratory judgment action within a reasonable time after the action is filed, University may prosecute the infringement or answer the declaratory judgment action under its sole control and at its sole expense, and any recovery obtained shall be given to University. If University takes action under this Subsection 6.4(d), University shall keep Company reasonably informed of material actions taken by University with respect to the infringement or declaratory action, provided that, University may not enter into any Settlement of such infringement or declaratory judgment action if such Settlement would create a financial obligation for or admission of liability by Company, without the prior written consent of Company, which consent may not be unreasonably withheld or delayed.

(e) Cooperation. Both parties shall cooperate fully in any action under this Section 6.4. which is controlled by the other party, provided that the controlling party reimburses the cooperating party promptly for any reasonable costs and expenses incurred by the cooperating party in connection with providing assistance.

7. Confidential Information; Publications; Publicity.

7.1. Confidential Information.

(a) Designation. The Disclosing Party shall mark Confidential Information that is disclosed in writing with a legend indicating its confidential status (such as, "Confidential" or "Proprietary"). The Disclosing party shall document Confidential Information that is disclosed orally or visually in a written notice and deliver the notice to the Receiving Party within [**] of the date of disclosure. The notice shall summarize the Confidential Information that was disclosed and reference the time and place of disclosure.

(b) Obligations. For [**] after disclosure of any portion of Confidential Information, the Receiving Party shall (i) maintain Confidential Information in confidence, except that the Receiving Party may disclose or permit the disclosure of any Confidential Information to its Affiliates, actual or potential Sublicensees, trustees or directors, officers, employees, contractors, consultants, and advisors who are obligated to maintain the confidential nature of Confidential Information and who need to know Confidential Information for the purposes of this Agreement, or with respect to any of the parties, to its actual or potential investors, collaborators, acquirers or financing sources who have a need to know the Confidential Information and who are subject to substantially similar obligations of confidentiality and non-use; (ii) use Confidential Information solely for the purposes of this Agreement; and (iii) allow its Affiliates, Sublicensees, trustees or directors, officers, employees, contractors, consultants, and advisors, and in the case of Company, investors, collaborators, acquirers and financing sources, to reproduce the Confidential Information only to the extent necessary for the purposes of this Agreement, with all reproductions being Confidential Information.

(c) Exceptions. The obligations of the Receiving Party under Subsection 7.1(b) do not apply to the extent that the Receiving Party can demonstrate that Confidential Information (i) was in the public domain prior to the time of its disclosure under this Agreement; (ii) entered the public domain after the time of its disclosure under this Agreement through means other than an unauthorized disclosure resulting from an act or omission by the Receiving Party; (iii) was already known or independently developed or discovered by the Receiving Party without use of the Confidential Information; (iv) is or was disclosed to the Receiving Party at any time, whether prior to or after the time of its disclosure under this Agreement, by a Third Party having no obligation of confidentiality with respect to the Confidential Information; or (v) is required to be disclosed to comply with applicable laws or regulations or with a court or administrative order, provided that the Disclosing Party receives reasonable prior written notice of the disclosure.

(d) Ownership and Return. The Receiving Party acknowledges that the Disclosing Party (or a Third Party entrusting its own information to the Disclosing Party) owns the Confidential Information in the possession of the Receiving Party subject, in the case of Licensed Know-How, to the license granted hereunder. Upon expiration or termination of this Agreement, or at the request of the Disclosing Party, the Receiving Party shall return to the Disclosing Party all originals, copies, and summaries of documents, materials, and other tangible manifestations of Confidential Information in the possession or control of the Receiving Party, except that the Receiving Party may retain one copy of the Confidential Information in the possession of its legal counsel solely for the purpose of monitoring its obligations under this Agreement. Notwithstanding the foregoing, Company may retain Licensed Know-How (and any copies and summaries of documents, materials, and other tangible manifestations thereof) subject to the license granted hereunder during the term of this Agreement and following expiration (but not early termination) of this Agreement.

7.2. Publicity Restrictions. Company may not use the name of University or any of its trustees, officers, faculty, students, employees, or agents, or any adaptation of their names, or any terms of this Agreement in any promotional material or other public announcement or disclosure without the prior written consent of University.

The foregoing notwithstanding, Company may without the consent of University (a) disclose that information, including the terms of this Agreement, in any prospectus, offering memorandum, or other document or filing required by applicable securities laws or other applicable law or regulation, provided that Company provides University at least [**] (or a shorter period in order to enable Company to make a timely announcement to fulfill applicable securities laws or other applicable law or regulation, while affording University the maximum feasible time to review the announcement) prior written notice of the proposed text for the purpose of giving University the opportunity to comment on the text, and (b) identify University as needed to convey that this Agreement and the licenses hereunder exist.

8. Term and Termination.

8.1. Term. This Agreement commences on the Effective Date and remains in effect until the expiration of the Royalty Term (see Section 4.5) unless earlier terminated in accordance with the provisions of this Agreement. Upon the expiration of the Royalty Term, the licenses granted to Company hereunder shall automatically become perpetual, royalty-free, fully paid up and irrevocable.

8.2. Voluntary Termination by Company. Company may terminate this Agreement for any reason upon ninety (90) days' prior written notice to University; provided, however that if Company elects to terminate this Agreement during the Royalty Term, Company agrees that it shall lose all rights hereunder to make, use, sell, have made, have used or have sold Licensed Products.

8.3. Termination for Default. If either party commits a material breach of its obligations under this Agreement and fails to cure that breach within [**] after receiving written notice of the breach, the other party may terminate this Agreement immediately upon written notice to the party in breach. Notwithstanding the foregoing, if Company commits a breach of its payment obligations under this Agreement and fails to cure the breach within the applicable cure periods as specified under subparts (a), (b) or (c) of this Section 8.3, which cure periods begin upon delivery of notice of breach by University to Company, University may terminate this Agreement upon written notice to Company: (a) [**] following the first notice of payment breach, (b) [**] following the second notice of a payment breach, (c) [**] following the third notice of a payment breach, and (d) immediately upon receipt of the fourth or subsequent notice of a payment breach, for which no cure period will be available. In addition, following the third notice of an uncured payment breach, any subsequent material breach by Company will entitle University to terminate this Agreement immediately upon written notice to Company, without any cure period. For avoidance of doubt, with respect to any purported payment obligation that is disputed by Company in good faith, Company's non-payment with respect to such purported payment obligation shall not be considered a breach.

8.4. Force Majeure. Neither party is responsible for delays resulting from causes beyond its reasonable control, including without limitation fire, explosion, flood, war, strike, act of terrorism or riot, provided that the nonperforming party uses commercially reasonable efforts to remove those causes of nonperformance and continues performance under this Agreement with reasonable dispatch whenever the causes are removed.

8.5. Effect of Termination. The following provisions survive the termination of this Agreement: Articles 1 and 9; Sections 3.3., 3.4., 3.6(b)., 5.2. (obligation to provide final report and payment), 5.3., 5.4., 5.5., 5.6., 5.7., 5.8., 6.3. (but only for patent-related expenses incurred until date of termination), 7.1., 7.2., 8.5., 10.7., 10.8., 10.9. and 10.10. Upon the early termination of this Agreement, Company and its Affiliates and Sublicensees may complete and sell any work-in-progress and inventory of Licensed Products that exist as of the effective date of termination, provided that (a) Company is current in payment of all amounts due University under this Agreement, (b) Company pays University the applicable royalty and Sublicense Income on sales of Licensed Products in accordance with the terms of this Agreement, and (c) Company and its Affiliates and Sublicensees complete and sell all work-in-progress and inventory of Licensed Products within [**] after the effective date of termination. Furthermore, upon any early termination of this Agreement, Company shall have the right to elect that any then-existing Sublicense Agreements survive as direct licenses from University (so long as the applicable Sublicensees are not in breach of any material obligation under this Agreement and its Sublicense Agreement) and University will accept any such survival elected by Company, provided however such Sublicense Agreement is modified to reflect University's status as a tax exempt agency of the Commonwealth of Massachusetts (e.g., state law,

indemnification). Each surviving Sublicense Agreement will remain in full force and effect with University as the licensor instead of Company, but the duties and obligations of University under the surviving Sublicense Agreement will not be greater than those of the University under this Agreement and the rights of University under the Sublicense Agreement will not be less than its rights under this Agreement.

9. Dispute Resolution.

9.1. Procedures Mandatory. The parties shall resolve any dispute arising out of or relating to this Agreement solely by means of the procedures set forth in this Article. These procedures constitute legally binding obligations that are an essential provision of this Agreement. If either party fails to observe the procedures of this Article, as modified by their written agreement, the other party may bring an action for specific performance in any court of competent jurisdiction.

9.2. Dispute Resolution Procedures.

(a) Negotiation. In the event of any dispute arising out of or relating to this Agreement, the affected party shall notify the other party, and the parties shall attempt in good faith to resolve the matter within [**] after the date of notice (the "Notice Date"). Any disputes not resolved by good faith discussions shall be referred to senior executives of each party, who shall meet at a mutually acceptable time and location within [**] after the Notice Date and attempt to negotiate a settlement.

(b) Mediation. If the matter remains unresolved within [**] after the Notice Date, or if the senior executives fail to meet within [**] after the Notice Date, either party may initiate mediation upon written notice to the other party, and both parties shall engage in a mediation proceeding under the then current CPR Institute for Dispute Resolution ("CPR") Model Procedure for Mediation of Business Disputes. Specific provisions of this Subsection 9.2(b) override inconsistent provisions of the CPR Model Procedure. The parties shall select the mediator from the CPR Panels of Neutrals. If the parties cannot agree upon the selection of a mediator within [**] after the Notice Date, then upon the request of either party, the CPR shall appoint the mediator. The parties shall attempt to resolve the dispute through mediation until one of the following occurs: (i) the parties reach a written settlement; (ii) the mediator notifies the parties in writing that they have reached an impasse; (iii) the parties agree in writing that they have reached an impasse; or (iv) the parties have not reached a settlement within [**] after the Notice Date.

(c) Trial Without Jury. If the parties fail to resolve the dispute through mediation, or if neither party elects to initiate mediation within [**] of the Notice Date, each party may, subject to Section 10.9, pursue any other remedies legally available to resolve the dispute. However, THE PARTIES EXPRESSLY WAIVE THE RIGHT TO A JURY TRIAL in any legal proceeding under this Subsection 9.2(c).

9.3. Preservation of Rights Pending Resolution.

(a) Performance to Continue. Each party shall continue to perform its obligations under this Agreement pending final resolution of any dispute arising out of or relating to this Agreement. However, a party may suspend performance of its obligations during any period in which the other party fails or refuses to perform its obligations.

(b) Provisional Remedies. Although the procedures specified in this Article are the exclusive procedures for resolution of disputes arising out of or relating to this Agreement, either party may seek a preliminary injunction or other equitable relief if, in its reasonable judgment, that action is necessary to avoid irreparable harm to itself or to preserve its rights under this Agreement.

(c) Statute of Limitations. The parties agree that all applicable statutes of limitation and time-based defenses (such as, estoppel and laches) are tolled while the procedures set forth in Subsections 9.2(a) and 9.2(b) are pending. The parties shall take any actions necessary to effectuate this result.

10. Representations and Warranties; Miscellaneous.

10.1. IP Representations and Warranties. University represents that (a) its employees have assigned to University their entire right, title, and interest in the Patent Rights and Biological Materials, and that it has authority to grant the rights and licenses set forth in this Agreement, (b) every person who may be involved in the development of the Patent Rights and Biological Materials has signed the University Participation Agreement, which assigns to University all rights in the Patent Rights and commercial rights in the Biological Materials, (c) to its knowledge, for any federal government-funded inventions claimed by the Patent Rights, University has made all notifications required under the Patent and Trademark Law Amendments Act of 1980 (Public Law 96-518; 35 U.S.C. 200-212), including any amendments thereto and all regulations promulgated thereunder, and (d) it has not granted any rights in the Patent Rights, Biological Materials or Licensed Know-How to any Third Party or University Affiliate that is inconsistent with the grant of rights in this Agreement. UNIVERSITY MAKES NO OTHER WARRANTIES CONCERNING THE PATENT RIGHTS, INCLUDING WITHOUT LIMITATION ANY EXPRESS OR IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. Specifically, University makes no warranty or representation (i) regarding the validity or scope of the Patent Rights, (ii) that the exploitation of the Patent Rights or any Licensed Product will not infringe any patents or other intellectual property rights of a Third Party, and (iii) that any Third Party is not currently infringing or will not infringe the Patent Rights.

10.1.1 Company's Representations and Warranties. Company hereby represents to University as forth below.

(a) Organization and Standing. Company is a corporation duly organized, validly existing and in good standing under the laws of the State of Delaware and has all requisite corporate power and authority to carry on its businesses as now conducted. Company is qualified or licensed to do business as a foreign corporation in all jurisdictions where such qualification or licensing is required, except where the failure to be so qualified or in good standing or have such power or authority would not, individually or in the aggregate, have a material adverse effect upon Company.

(b) Corporate Power and Authority; Valid and Binding Agreement. Company has all requisite power and authority to enter into this Agreement and to issue the Shares. This Agreement is a valid and binding obligation of Company enforceable against Company in accordance with its terms, except as the same may be limited by (i) bankruptcy, insolvency, moratorium, and other laws of general application affecting the enforcement of creditors' rights or (ii) laws related to the availability of specific performance, injunctive relief or other equitable remedies.

(c) Valid Issuance. The Shares, when issued in compliance with the provisions of this Agreement, will be duly authorized, validly issued, fully paid and nonassessable and will be free of any liens or encumbrances caused or created by Company, other than, in each case, restrictions imposed by this Agreement and applicable securities laws.

(d) Offering. Subject to the truth and accuracy of University's representations set forth in Section 10.1.2 of this Agreement, the issuance of the Shares as contemplated by this Agreement is in compliance with applicable federal securities laws.

10.1.2 University's Representations and Warranties. University hereby represents to Company as forth below.

(a) Organization and Standing. University is a not-for-profit, public institution of higher education duly organized, validly existing and in good standing under the laws of the Commonwealth of Massachusetts and has all requisite power and authority to carry on its businesses as now conducted.

(b) Power and Authority; Valid and Binding Agreement. University has all requisite power and authority to enter into this Agreement and to acquire the Shares. This Agreement is a valid and binding obligation of

University enforceable against University in accordance with its terms, except as the same may be limited by (i) bankruptcy, insolvency, moratorium, and other laws of general application affecting the enforcement of creditors' rights or (ii) laws related to the availability of specific performance, injunctive relief or other equitable remedies.

(c) Not an Underwriter. University acknowledges that the Shares to be issued hereunder shall be received by University for its own account, not as a nominee or agent, and not with a view to the resale or distribution of any part thereof. University can bear the economic risk of holding the Shares indefinitely and a total loss with respect to such investment.

(d) Disclosure of Information. University has received or has had full access to all the information from Company and its management that University considers necessary or appropriate for deciding whether to consummate an investment in the Shares. University further represents that it has had an opportunity to ask questions and receive answers from Company regarding Company, its financial condition, results of operations and prospects and the terms and conditions of the offering of the Shares sufficient to enable it to evaluate its investment.

(e) Status. University is a public institution of higher learning and agency of the Commonwealth of Massachusetts established under the Massachusetts General Laws Part 1, Title XII, Chapter 75 § 1 and is a tax exempt state agency under the doctrine of intergovernmental tax immunity and has total assets in excess of $5,000,000. University has such knowledge and experience in financial or business matters that it is capable of evaluating the merits and risks of owning the Shares.

(f) No “Bad Actor” Disqualification. University has not taken any of the actions set forth in, and is not subject to, the disqualification provisions of Rule 506(d)(1) of the Securities Act of 1933, as amended.

(g) Securities Laws. University represents that it is familiar with Rule 144 of the Securities Act (“Rule 144”), as presently in effect. University acknowledges that it is responsible for making any securities filings imposed on it under Sections 13 and 16 of the Securities Exchange Act of 1934, as amended, on account of its and its Affiliates’ ownership of securities of the Company and any transactions with respect thereto.

(h) Restricted Securities; Legends. University understands that the Shares, when issued, shall be “restricted securities” under the federal securities laws, and, as such, any certificates representing the Shares shall bear the following legends:

(A) “These securities have not been registered under the Securities Act of 1933. They may not be sold, offered for sale, pledged or hypothecated in the absence of a registration statement in effect with respect to the securities under the Securities Act or an opinion of counsel (which counsel shall be reasonably satisfactory to the Company) that such registration is not required or unless sold pursuant to Rule 144 of the Securities Act.”; and

(B) any legend required by applicable state securities laws.

10.1.3. Removal of Legends. The parties hereby acknowledge and agree as follows:

(a) Certificates evidencing the Shares shall not contain the legend set forth in Section 10.1.2(h)(A): (i) following a sale of such Shares pursuant to a registration statement covering the resale of such Shares, while such registration statement is effective under the Securities Act, (ii) following any sale, distribution or other disposition of such Shares pursuant to Rule 144 or (iii) if such Shares are eligible for sale, distribution or disposition under Rule 144, without the requirement for Company to be in compliance with the current public information required under Rule 144 as to such Shares and without volume or manner-of-sale restrictions under Rule 144.

(b) Company agrees that at such time as any legend set forth in Section 10.1.2(i) is no longer required under this Section 10.1.3, Company will, no later than [**] following the delivery by University to

Company or notice by University to Company of delivery by University to the transfer agent for the Shares of a certificate representing Shares issued with such legend (together with any legal opinion required by the transfer agent), deliver or cause to be delivered to University a certificate representing such Shares that is free from such legend, or, in the event that such shares are uncertificated, remove any such legend in Company's stock records.

10.2. Compliance with Law and Policies. Company agrees to comply with applicable law and the applicable policies of University in the area of technology transfer of which the Company is aware and shall promptly notify University of any violation that Company knows or has reason to believe has occurred or is likely to occur. The University policies currently in effect at the Worcester campus are the Intellectual Property Policy, Policy on Conflicts of Interest Relating to Intellectual Property and Commercial Ventures, and Policy on Faculty Consulting and Outside Activities at https://umassmed.edu/bridge/Inventors/forms-policies-and-agreements/, each of which are accessible to the Company at https://www.umassmed.edu/ofa/governance-policies/coi/.

10.3. Tax-Exempt Status. Company acknowledges that University, as a public institution of the Commonwealth of Massachusetts, is an exempt organization under the United States Internal Revenue Code of 1986, as amended. Company also acknowledges that certain facilities in which the licensed inventions were developed may have been financed through offerings of tax-exempt bonds. If the Internal Revenue Service determines, or if counsel to University reasonably determines, that any term of this Agreement jeopardizes the tax-exempt status of University or the bonds used to finance University facilities, the relevant term is invalid and shall be modified in accordance with Section 10.11.

10.4. Counterparts. This Agreement may be executed in one or more counterparts, each of which is an original, and all of which together are one instrument.

10.5. Headings. All headings are for convenience only and do not affect the meaning of any provision of this Agreement.

10.6. Binding Effect. This Agreement is binding upon and inures to the benefit of the parties and their respective permitted successors and assigns.

10.7. Assignment. University may not assign this Agreement or any rights or obligations hereunder to any Third Party without the prior written consent of the Company, which consent may not be unreasonably withheld or delayed. University may without consent of the Company assign this Agreement and the rights and obligations hereunder to an Affiliate of University. Furthermore, University may not assign all or substantially all of the Patent Rights, Biological Materials or Licensed Know-How licensed hereunder without assigning this Agreement to the same assignee. Company may freely assign this Agreement and the rights and obligations hereunder, provided that in no event shall the Company (or any successor), without the prior written consent of University, delegate all or substantially all of its obligations hereunder to an entity without assigning all or substantially all of its rights hereunder to the same entity.

10.8. Amendment and Waiver. The parties may only amend, supplement, or otherwise modify this Agreement through a written instrument signed by both parties. The waiver of any rights or failure to act in a specific instance relates only to that instance and is not an agreement to waive any rights or fail to act in any other instance.

10.9. Governing Law. This Agreement is governed by and construed in accordance with the laws of the Commonwealth of Massachusetts irrespective of any conflicts of law principles. The parties may only bring legal action that arises out of or in connection with this Agreement in the Massachusetts Superior Court in Suffolk County.

10.10. Notice. Any notices required or permitted under this Agreement shall be in writing, shall specifically refer to this Agreement, and shall be sent by recognized national overnight courier, or registered or certified mail, postage prepaid, return receipt requested, to the following addresses:

If to University: **If to Company:**

Office of Technology Management
University of Massachusetts
55 Lake Avenue North, S4-110
Worcester, MA 01655-0002
Attention: Executive Director

IVERIC bio, Inc.
One Penn Plaza, Suite 3520
New York, NY 10119
Attention: Legal Department

With a copy to (which shall not constitute notice):
WilmerHale LLP
60 State Street
Boston, MA 02109
Attn: Steven D. Barrett, Esq.

All notices under this Agreement are effective upon receipt. A party may change its contact information immediately upon written notice to the other party in the manner provided in this Section 10.10.

10.11. Severability. If any provision of this Agreement is held invalid or unenforceable for any reason, the invalidity or unenforceability does not affect any other provision of this Agreement, and the parties shall negotiate in good faith to modify the Agreement to preserve (to the extent possible) their original intent. If the parties fail to reach a modified agreement within [**] after the relevant provision is held invalid or unenforceable, then the dispute shall be resolved in accordance with the procedures set forth in Article 9. While the dispute is pending resolution, this Agreement shall be construed as if the provision were deleted by agreement of the parties.

10.12. Entire Agreement. This Agreement constitutes the entire agreement between the parties with respect to its subject matter and supersedes all prior agreements or understandings between the parties relating to its subject matter. However, any sponsored research agreement and/or material transfer agreement entered into between the parties relating to the subject matter hereof shall remain in full force and effect in accordance with their respective terms.

[remainder of page intentionally left blank]

The parties have caused this Agreement to be executed by their duly authorized representatives as of the Effective Date.

UNIVERSITY OF MASSACHUSETTS **IVERIC BIO, INC.**

By: /s/ James P. McNamara
Name: James P. McNamara, Ph.D.,
Title: Executive Director,
Office of Technology Management

By: /s/ Glenn P. Sblendorio
Name: Glenn P. Sblendorio
Title: CEO & President

UNIVERSITY OF PENNSYLVANIA

AMENDMENT NO. 1 TO MASTER SPONSORED RESEARCH AGREEMENT

This Amendment No. 1 to the Master Sponsored Research Agreement ("**Agreement**") by and between The Trustees of the University of Pennsylvania, a Pennsylvania nonprofit corporation ("**Penn**"), with offices located at Penn Center for Innovation, 3600 Civic Center Blvd., 9th Floor, Philadelphia, PA 19104-4310, and IVERIC bio, Inc. (formerly Ophthotech Corporation), a Delaware corporation ("**Sponsor**"), having a place of business at One Penn Plaza, Suite 3520, New York, NY 10119 is dated as of October 1, 2019 (the "**Amendment No. 1 Effective Date**"). Penn and Sponsor may be referred to herein as a "**Party**" or, collectively, as "**Parties**".

RECITALS:

WHEREAS, the Parties entered into a Master Sponsored Research Agreement dated October 30, 2018 ("**Agreement**"). Capitalized terms used but not defined herein shall have the meanings ascribed to them in the Agreement; and

WHEREAS, the Parties now desire to amend the Agreement as set forth herein.

NOW, THEREFORE, in consideration of the various promises and undertakings set forth herein, the Parties agree as follows:

1. The following shall be added to the end of Section 6.2 of the Agreement titled "Penn Intellectual Property":

   The foregoing notwithstanding, Penn acknowledges that Sponsor, as a public company, may from time to time wish to disclose the outcome and conclusions of Research Results from one or more SOWs. Before making any such disclosure, Sponsor shall provide Penn with a copy of the disclosure, along with an identification of third parties to whom such disclosure would be made, for Penn's review and consideration. Penn has the right to decline any such request in its discretion; provided that Penn agrees that it will consider any request hereunder in good faith and that it will not unreasonably withhold its consent to any such request.

2. The Agreement, including any Exhibits and as amended by this Amendment, constitutes and contains the entire understanding and agreement of the Parties respecting the subject matter hereof and cancel and supersedes any and all prior negotiations, correspondence, understandings and agreements between the Parties, whether oral or written, regarding such subject matter. No waiver, modification or amendment of any provision of the Agreement and/or this Amendment shall be valid or effective unless made in a writing referencing the Agreement and/or this Amendment and signed by a duly authorized officer of each Party.

3. This Amendment may be executed in counterparts, each of which will be deemed an original, and all of which together will be deemed to be one and the same instrument. A portable document format (PDF) or electronic copy of this Amendment, including the signature pages, will be deemed an original.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the duly authorized representatives of the Parties hereby execute this Amendment as of the date first written above.

THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA	**IVERIC BIO, INC.**
By: /s/ Christine S. Baxter	By: /s/ Todd Anderman
Name: Christine S. Baxter	Name: Todd Anderman
Title: Sr Assoc. Dir., Corp. Contracts	Title: VP & General Counsel

UNIVERSITY OF PENNSYLVANIA

AMENDMENT NO. 1 TO MASTER SPONSORED RESEARCH AGREEMENT

This Amendment No. 1 to the Master Sponsored Research Agreement ("**Agreement**") by and between The Trustees of the University of Pennsylvania, a Pennsylvania nonprofit corporation ("**Penn**"), with offices located at Penn Center for Innovation, 3600 Civic Center Blvd., 9th Floor, Philadelphia, PA 19104-4310, and IVERIC bio, Inc. (formerly Ophthotech Corporation), a Delaware corporation ("**Sponsor**"), having a place of business at One Penn Plaza, Suite 3520, New York, NY 10119 is dated as of October 1, 2019 (the "**Amendment No. 1 Effective Date**"). Penn and Sponsor may be referred to herein as a "**Party**" or, collectively, as "**Parties**".

RECITALS:

WHEREAS, the Parties entered into a Master Sponsored Research Agreement dated June 6, 2018 ("**Agreement**"). Capitalized terms used but not defined herein shall have the meanings ascribed to them in the Agreement; and

WHEREAS, the Parties now desire to amend the Agreement as set forth herein.

NOW, THEREFORE, in consideration of the various promises and undertakings set forth herein, the Parties agree as follows:

1. The following shall be added to the end of Section 6.2 of the Agreement titled "Penn Intellectual Property":

   The foregoing notwithstanding, Penn acknowledges that Sponsor, as a public company, may from time to time wish to disclose the outcome and conclusions of Research Results from one or more SOWs. Before making any such disclosure, Sponsor shall provide Penn with a copy of the disclosure, along with an identification of third parties to whom such disclosure would be made, for Penn's review and consideration. Penn has the right to decline any such request in its discretion; provided that Penn agrees that it will consider any request hereunder in good faith and that it will not unreasonably withhold its consent to any such request.

2. The Agreement, including any Exhibits and as amended by this Amendment, constitutes and contains the entire understanding and agreement of the Parties respecting the subject matter hereof and cancel and supersedes any and all prior negotiations, correspondence, understandings and agreements between the Parties, whether oral or written, regarding such subject matter. No waiver, modification or amendment of any provision of the Agreement and/or this Amendment shall be valid or effective unless made in a writing referencing the Agreement and/or this Amendment and signed by a duly authorized officer of each Party.

3. This Amendment may be executed in counterparts, each of which will be deemed an original, and all of which together will be deemed to be one and the same instrument. A portable document format (PDF) or electronic copy of this Amendment, including the signature pages, will be deemed an original.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the duly authorized representatives of the Parties hereby execute this Amendment as of the date first written above.

THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA	**IVERIC BIO, INC.**
By: /s/ Christine S. Baxter	By: /s/ Todd Anderman
Name: Christine S. Baxter	Name: Todd Anderman
Title: Sr Assoc. Dir., Corp. Contracts	Title: VP & General Counsel

Exhibit 31.1

CERTIFICATIONS

I, Glenn P. Sblendorio, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q for the quarter ended September 30, 2019 of IVERIC bio, Inc.;

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 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 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: November 12, 2019

By: /s/ Glenn P. Sblendorio

Glenn P. Sblendorio
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, David F. Carroll, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q for the quarter ended September 30, 2019 of IVERIC bio, Inc.;

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 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 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: November 12, 2019

By: /s/ David F. Carroll

David F. Carroll
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

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 IVERIC bio, Inc. (the "Company") for the period ended September 30, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Glenn P. Sblendorio, Chief Executive Officer of the Company, hereby certifies, pursuant to Rule 13a-14(b) and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; 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: November 12, 2019

By: /s/ Glenn P. Sblendorio

Glenn P. Sblendorio
Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

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 IVERIC bio, Inc. (the "Company") for the period ended September 30, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, David F. Carroll, Chief Financial Officer of the Company, hereby certifies, pursuant to Rule 13a-14(b) and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; 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: November 12, 2019

By: /s/ David F. Carroll

David F. Carroll
Chief Financial Officer
(Principal Financial Officer)