As Filed Pursuant to Rule 424(b)(5)
Registration No. 333-226497

PROSPECTUS SUPPLEMENT (Subject to Completion) **Dated June 17, 2020**

$50,000,000

Common Stock
Pre-Funded Warrants to Purchase Common Stock

We are offering $50.0 million of shares of our common stock and, in lieu of common stock to certain investors that so choose, pre-funded warrants to purchase $ million of shares of our common stock. The purchase price of each pre-funded warrant will equal the price per share at which shares of our common stock are being sold to the public in this offering, minus $0.001, and the exercise price of each pre-funded warrant will equal $0.001 per share. This prospectus supplement also relates to the offering of the shares of our common stock issuable upon the exercise of such pre-funded warrants.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "ISEE". On June 16, 2020, the last reported sale price of our common stock on The Nasdaq Global Select Market was $4.46 per share. There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on The Nasdaq Global Select Market or any other national securities exchange or nationally recognized trading system.

Concurrently with this offering, pursuant to a stock purchase agreement with affiliates of Vivo Capital, LLC and Samsara BioCapital, LP, or the private placement purchasers, dated June 17, 2020, or the private placement agreement, we have agreed to sell to the private placement purchasers, in a private placement exempt from the registration requirements of the Securities Act of 1933, as amended, and at a sale price equal to the price to the public in this offering, approximately $35 million of shares of our common stock, or the concurrent private placement. Cowen and Company, LLC and Credit Suisse Securities (USA) LLC are serving as placement agents for the concurrent private placement and will receive a placement agent fee equal to a percentage of the total purchase price of the shares of our common stock sold in the concurrent private placement, which percentage will be equal to the percentage discount the underwriters will receive on the shares of our common stock and pre-funded warrants sold in this offering. The consummation of the concurrent private placement is contingent on the closing of this offering and the satisfaction of certain other customary conditions. However, the consummation of this offering is not contingent on the consummation of the concurrent private placement.

Our business and an investment in our common stock involve significant risks. These risks are described under the caption "Risk Factors" beginning on page S-7 of this prospectus.

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

	Per Share	*Per Pre-Funded Warrant*	*Total*
Public offering price	**$**	**$**	**$**
Underwriting discounts	**$**	**$**	**$**
Proceeds, before expenses, to IVERIC bio, Inc.	**$**	**$**	**$**

The underwriters may also purchase up to an additional $ million of shares of our common stock from us at the public offering price, less the underwriting discount, within 30 days from the date of the prospectus.

The underwriters expect to deliver the shares against payment in New York, New York on June , 2020. The pre-funded warrants are expected to be delivered against payment on June , 2020.

Book-Running Managers

Cowen **Credit Suisse**

Lead Manager

Wedbush PacGrow

Prospectus dated June , 2020

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PROSPECTUS SUPPLEMENT

PROSPECTUS

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering and adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Neither we nor the underwriters have authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement, in the accompanying prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. Neither we nor the underwriters take any responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you.

This prospectus supplement, the accompanying prospectus and any such free writing prospectus do not constitute an offer to sell, or a solicitation of an offer to purchase, the securities offered by this prospectus supplement, the accompanying prospectus and any such free writing prospectus in any jurisdiction to or from any person to whom or from whom it is unlawful to make such offer or solicitation of an offer in such jurisdiction. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and in any free writing prospectus that we have authorized for use in connection with this offering is accurate only as of the date of those respective documents. It is important for you to read and consider all information contained in this prospectus supplement and in the accompanying prospectus, including the documents incorporated by reference herein and therein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections entitled "Where You Can Find More Information" and "Incorporation by Reference" in this prospectus supplement and in the accompanying prospectus.

Other than in the United States, no action has been taken by us that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except

under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement and accompanying prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement and accompanying prospectus.

Unless otherwise indicated or the context otherwise requires, references in this prospectus supplement and the accompanying prospectus to "IVERIC," "we," "our," "us," and "the Company" refer, collectively, to IVERIC bio, Inc., a Delaware corporation, and its consolidated subsidiaries, or any one or more of them as the context may require. When we refer to "you" in this prospectus supplement, we mean all purchasers of the securities being offered by this prospectus supplement and the accompanying prospectus, whether they are the holders or only indirect owners of those securities.

The trademarks, trade names and service marks appearing in this prospectus supplement and accompanying prospectus are the property of their respective owners. We have omitted the ® and ™ designations, as applicable, for the trademarks named in this prospectus supplement and accompanying prospectus.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the information incorporated by reference in this prospectus supplement and the accompanying prospectus include "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities and Exchange Act of 1934, as amended, or the Exchange Act. All statements, other than statements of historical facts, contained in this prospectus supplement and the accompanying prospectus, and the information incorporated by reference herein and therein, 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 prospectus supplement 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;
- the effects of the novel coronavirus (COVID-19) pandemic and related response measures on our business and operations, including the timing, costs, conduct and outcome of our research and development programs, and financial position;
- our expectations regarding the impact of results from our OPH2003 pivotal clinical trial evaluating Zimura for the treatment of geographic atrophy secondary to 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;
- the timing, costs, conduct and outcome of ISEE2008, our planned Phase 3 clinical trial evaluating Zimura for the treatment of geographic atrophy secondary to age-related macular degeneration, and expectations regarding the potential for Zimura to receive regulatory approval for the treatment of geographic atrophy secondary to age-related macular degeneration based on the clinical trial results we have received to date and future results from the ISEE2008 clinical trial and any other trials we may conduct;
- our ability to establish and maintain arrangements and capabilities for the manufacture of our therapeutics and gene therapy product candidates, including scale up and validation of the manufacturing process for Zimura;
- 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 clinical trials, including statements regarding the timing of the initiation and completion of, and the receipt of results from, such clinical trials, the costs to conduct such clinical trials, and the impact of the results of such clinical trials on our business strategy;
- the timing, costs, conduct and outcome of our ongoing and planned research and preclinical development activities, including statements regarding the timing of the initiation and completion of, and the receipt of results from, such activities, the costs to conduct such activities, and the impact of the results of such activities on our business strategy;
- the potential advantages of our product candidates and other technologies that we are pursuing, including the advantages and limitations of inhibition of complement factor C5 and

HtrA1, including our hypotheses regarding complement inhibition as a mechanism of action to treat geographic atrophy, and of gene therapy, including the use of minigenes;

- our estimates regarding the number of patients affected by the diseases our product candidates and development programs are intended to treat;
- 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 potential collaboration or out-licensing opportunities for further 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;
- 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;
- our competitive position; and
- our expectations related to our use of proceeds from this offering, the concurrent private placement and our existing cash resources.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you 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. See the "Risk Factors" section of this prospectus supplement and the accompanying prospectus, the risk factors included in our periodic reports filed with the Securities and Exchange Commission, or the SEC, and in the other documents incorporated by reference in this prospectus supplement and the accompanying prospectus for more information. 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 prospectus supplement and the accompanying prospectus, and the documents incorporated by reference herein and therein, completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements except as required by applicable law.

This prospectus supplement and the accompanying prospectus include statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere in this prospectus supplement and the accompanying prospectus and in the documents incorporated by reference herein and therein. This summary does not contain all of the information you should consider before investing in our common stock or pre-funded warrants. You should read this entire prospectus supplement and the accompanying prospectus carefully, especially the risks of investing in our common stock or pre-funded warrants discussed under "Risk Factors" beginning on page S-7 of this prospectus supplement and in our periodic and other reports filed with the SEC, along with our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision.

IVERIC BIO, INC.

Our Business

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.

Our therapeutics portfolio consists of Zimura® (avacincaptad pegol), a complement C5 inhibitor, and our preclinical development program of High temperature requirement A serine peptidase 1 protein, or HtrA1, inhibitors. We are currently targeting the following diseases with Zimura:

- geographic atrophy, or GA, which is the advanced stage of age-related macular degeneration, or AMD, and is characterized by marked thinning or atrophy of retinal tissue, leading to irreversible loss of vision; and
- autosomal recessive Stargardt disease, or STGD1, which is characterized by progressive damage to the central portion of the retina, or the macula, and other retinal tissue of young adults, leading to loss of vision.

On June 15, 2020, we announced positive 18-month results from our international, randomized, double masked, sham controlled, multi-center Phase 2/3 clinical trial, or the OPH2003 trial, assessing the safety and efficacy of Zimura for the treatment of GA secondary to AMD. The 18-month data, including reduction in the mean rate of GA growth over 18 months, supports the previously announced 12-month data from this trial, at which time point Zimura met the pre-specified primary efficacy endpoint in reducing the rate of GA growth with statistical significance. In this trial, the treatment effect for Zimura was observed as early as 6 months, with an increase in the absolute difference of the mean change in GA growth for treatment with either Zimura 2 mg or Zimura 4 mg, as compared to sham, at each subsequent time point, suggesting the progressive benefit of continuous treatment with Zimura. Zimura maintained its favorable safety profile at 18 months with no reported Zimura related adverse events, no cases of endophthalmitis and a lower rate of choroidal neovascularization (CNV) than reported for C3 inhibition. The overall 18-month data may suggest a dose response relationship. We are currently preparing to initiate a second international, randomized, double masked, sham controlled, multi-center Phase 3 clinical trial, or the ISEE2008 trial, comparing Zimura 2 mg with sham for the treatment of GA secondary to AMD. We are planning to initiate patient enrollment in June 2020.

In addition, we have ongoing a randomized, double masked, sham controlled, multi-center Phase 2b clinical trial, or the OPH2005 trial, evaluating the safety and efficacy of Zimura for the treatment of STGD1. 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, and which we believe could potentially serve as a pivotal clinical trial. We initially completed enrollment for this trial in February 2019 with a total of 95 patients enrolled. Following this offering and the concurrent private placement, we plan to re-open enrollment in this trial to enroll up to approximately 50 additional patients, with the goal of retaining 120 patients for 18-month analysis as was initially intended in the protocol for the OPH2005 trial. Newly enrolled patients will be randomized to be treated with Zimura 4 mg or sham for 18 months, following which we would plan to analyze and announce data for all patients in the trial. We have been and expect to remain masked to the treatment condition of all patients in the trial. In addition, we have not reviewed and do not plan to review or analyze efficacy data for any patients in the trial, until the 18-month data has been collected and analyzed for all patients enrolled in the trial.

We are developing our HtrA1 inhibitor program for GA and potentially other age-related retinal diseases.

Our gene therapy portfolio consists of two product candidates in preclinical development and several ongoing collaborative sponsored research programs, each of which uses adeno-associated virus, or AAV, for gene delivery. These AAV mediated 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, which is characterized by severe bilateral loss of vision at or soon after birth;
- autosomal recessive Stargardt disease; and
- IRDs associated with mutations in the USH2A gene, which include Usher syndrome type 2A, and USH2A-associated nonsyndromic autosomal recessive retinitis pigmentosa.

Our lead gene therapy product candidate is IC-100, which we are developing for the treatment of RHO-adRP. Subject to successful completion of preclinical development and manufacturing under current good manufacturing practices, or cGMP, we plan to file an investigational new drug application for IC-100 by the end of 2020 or early 2021 with the goal of starting patient enrollment in a Phase 1/2 clinical trial during the first half of 2021. We are also developing IC-200, our gene therapy product candidate for the treatment of IRDs associated with mutations in the *BEST1* gene. Subject to successful completion of preclinical development and manufacturing under cGMP and regulatory review, we expect to initiate a Phase 1/2 clinical trial for IC-200 during the first half of 2021.

Concurrent Private Placement

Concurrently with this offering, pursuant to the private placement agreement, we have agreed to sell to the private placement purchasers, in a private placement exempt from the registration requirements of the Securities Act and at a sale price equal to the price to the public in this offering, approximately $35 million of shares of our common stock. The consummation of the concurrent private placement is contingent on the closing of this offering and the satisfaction of certain other customary conditions. Pursuant to the terms and conditions of the private placement agreement, we

will be required to use commercially reasonable efforts to file a registration statement with the SEC on or before the date that is 60 days following the closing of the concurrent private placement and cause such registration statement to be declared effective within 90 days following the closing of the concurrent private placement (or under certain circumstances, 120 days following the closing of the concurrent private placement) for the resale of shares of our common stock purchased in the concurrent private placement. Cowen and Company, LLC and Credit Suisse Securities (USA) LLC are serving as placement agents for the concurrent private placement and will receive a placement agent fee equal to a percentage of the total purchase price of the shares of our common stock sold in the concurrent private placement, which percentage will be equal to the percentage discount the underwriters will receive on the shares of our common stock and pre-funded warrants sold in this offering. The closing of the concurrent private placement is expected to occur on or about June , 2020. The consummation of this offering is not contingent on the consummation of the concurrent private placement.

Company Information

We were incorporated under the laws of the State of Delaware on January 5, 2007 under the name Ophthotech Corporation. On April 15, 2019, we filed a certificate of amendment to our restated certificate of incorporation to change our corporate name from "Ophthotech Corporation" to "IVERIC bio, Inc." Our principal executive offices are located at One Penn Plaza, 35th Floor, New York, NY 10119, and our telephone number is (212) 845-8200. Our website address is www.ivericbio.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus supplement. We have included our website address in this prospectus supplement solely as an inactive textual reference.

THE OFFERING

Common stock offered by us	$50.0 million of shares of our common stock.
Pre-funded warrants offered by us	We are also offering, in lieu of common stock to certain investors that so choose, pre-funded warrants to purchase $ million of shares of our common stock. The purchase price of each pre-funded warrant will equal the price per share at which shares of common stock are being sold to the public in this offering, minus $0.001, and the exercise price of each pre-funded warrant will equal $0.001 per share. Each pre-funded warrant will be exercisable from the date of issuance until the date the warrant is exercised in full, subject to an ownership limitation. See "Description of Pre-Funded Warrants." This prospectus supplement also relates to the offering of the shares of common stock issuable upon the exercise of such pre-funded warrants.
Concurrent Private Placement	Concurrently with this offering, pursuant to the private placement agreement, we have agreed to sell to the private placement purchasers, in a private placement exempt from the registration requirements of the Securities Act and at a sale price equal to the price to the public in this offering, approximately $35 million of shares of our common stock. The consummation of the concurrent private placement is contingent on the closing of this offering and the satisfaction of certain other customary conditions. The private placement purchasers will receive certain registration rights upon the consummation of the concurrent private placement. Cowen and Company, LLC and Credit Suisse Securities (USA) LLC are serving as placement agents for the concurrent private placement and will receive a placement agent fee equal to a percentage of the total purchase price of the shares of our common stock sold in the concurrent private placement, which percentage will be equal to the percentage discount the underwriters will receive on the shares of our common stock and pre-funded warrants sold in this offering. The closing of the concurrent private placement is expected to occur on or about June , 2020. The consummation of this offering is not contingent on the consummation of the concurrent private placement.
Common stock to be outstanding after this offering and the concurrent private placement	shares.

Option to purchase additional shares	We have granted the underwriters an option for a period of 30 days to purchase up to an additional $ million of shares of our common stock. The number of shares subject to the underwriters' option will equal 15% of the total number of shares of common stock we are offering plus the shares underlying the pre-funded warrants.
Use of proceeds	We estimate that the net proceeds to us from this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately $ million (or approximately $ million if the underwriters exercise in full their option to purchase additional shares). We estimate that the net proceeds to us from the concurrent private placement, after deducting placement agent fees and estimated offering expenses payable by us, will be approximately $ million. We plan to use the net proceeds from this offering and the concurrent private placement to fund clinical development of, and to further develop our manufacturing capabilities for, Zimura, to fund preclinical research and development and potential clinical development of our gene therapy portfolio and HtrA1 inhibitor program, and for working capital and other general corporate purposes. See the "Use of Proceeds" section of this prospectus supplement for a more complete description of the intended use of proceeds from this offering and the concurrent private placement.
Risk Factors	You should read the "Risk Factors" section of this prospectus supplement beginning on page S-7 and in our periodic and other reports filed with the SEC, as well as those risk factors in the other documents incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of factors to consider carefully before deciding to purchase shares of our common stock or pre-funded warrants.
Nasdaq Global Select Market symbol	Our common stock is listed on The Nasdaq Global Select Market under the symbol "ISEE". There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on The Nasdaq Global Select Market or any other national securities exchange or nationally recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants will be limited. See "Description of Pre-Funded Warrants".

The number of shares of our common stock that will be outstanding immediately after this offering and the concurrent private placement as shown above is based on 51,334,897 shares of our common stock issued and outstanding as of June 15, 2020. The number of shares of our common stock that will be outstanding immediately after this offering and the concurrent private placement

assumes that none of the investors in this offering elect to purchase pre-funded warrants in lieu of common stock and excludes:

- 7,154,480 shares of our common stock issuable upon the exercise of stock options outstanding as of June 15, 2020, at a weighted average exercise price of $10.11 per share;
- 1,636,313 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of June 15, 2020;
- 2,773,913 additional shares of our common stock available for future issuance under our 2013 stock incentive plan;
- 897,250 additional shares of our common stock available for future issuance under our 2019 inducement stock incentive plan;
- 838,182 additional shares of our common stock available for future issuance under our 2016 employee stock purchase plan; and
- 2,250,000 shares of our common stock reserved for issuance upon the exercise of pre-funded warrants outstanding as of June 15, 2020.

Unless otherwise indicated or the context otherwise requires, all information in this prospectus supplement:

- assumes no exercise of the outstanding options and the outstanding pre-funded warrants described above;
- assumes no exercise by the underwriters of their option to purchase up to $ million of shares of common stock from us;
- assumes no exercise of the pre-funded warrants we are offering in this offering in lieu of common stock to certain investors; and
- does not give effect to potential future milestone payments payable in the form of shares of our common stock pursuant to (a) the agreement and plan of merger under which we acquired Inception 4, Inc., or the Inception 4 acquisition, in October 2018 or (b) the exclusive license agreement we entered into in July 2019 with the University of Massachusetts for rights to our miniCEP290 gene therapy program.

As of the date of this prospectus supplement, the sales agreement with Cowen and Company, LLC that we entered into on August 1, 2018 for our "at-the-market" equity offering program has been terminated and the "at-the-market" equity offering program pursuant to the sales agreement is no longer available to us.

RISK FACTORS

Investing in our common stock and pre-funded warrants involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this prospectus supplement, the accompanying prospectus and in the documents incorporated by reference herein and therein, including the risks described in our periodic and other reports filed with the Securities and Exchange Commission, or the SEC, before deciding to invest in our common stock or pre-funded warrants. If any of these risks actually occur, our business, prospects, operating results and financial condition could suffer materially. In such event, the trading price of our common stock could decline and you might lose all or part of your investment.

Risks Related to This Offering

If you purchase shares of common stock or pre-funded warrants in this offering, you will suffer immediate dilution of your investment.

The price of our common stock and pre-funded warrants in this offering is substantially higher than the net tangible book value per share of our outstanding common stock. Therefore, if you purchase shares of our common stock or pre-funded warrants in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering and the concurrent private placement. To the extent shares subsequently are issued under outstanding options or warrants, or to the extent that the pre-funded warrants being offered in this offering are exercised, you will incur further dilution. Based on a public offering price of $ per share of common stock and a public offering price of $ per pre-funded warrant, you will experience immediate dilution of $ per share of common stock and $ per pre-funded warrant, representing the difference between our as adjusted net tangible book value per share, after giving effect to this offering and the concurrent private placement, and the public offering prices.

We have broad discretion in the use of the net proceeds from this offering and the concurrent private placement and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and the concurrent private placement, including for any of the purposes described in the section of this prospectus supplement titled "Use of Proceeds," and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering and the concurrent private placement in a manner that does not produce income or that loses value.

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, 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, Inc. as upfront consideration for the Inception 4 acquisition. 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 could be freely sold and traded pursuant to a registration statement on Form S-3 (File No. 333-229978) that was declared effective by the SEC 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. Once registered on Form S-8, shares underlying these awards can be freely sold in the public market upon issuance, subject to volume, notice and manner of sale limitations applicable to affiliates.

We currently have on file with the SEC an effective universal shelf registration statement which allows us to offer and sell registered common stock, preferred stock, debt securities, depositary shares, units and/or warrants from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale. In addition, pursuant to the private placement agreement, we will be required to file a registration statement covering the sale of shares of our common stock purchased in the concurrent private placement subject to the terms and conditions of the private placement agreement. Once we register the offer and sale of such shares, the shares can be freely sold in the public market. See "Prospectus Supplement Summary—Concurrent Private Placement."

There is no public market for the pre-funded warrants being offered in this offering.

There is no public trading market for the pre-funded warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to list the pre-funded warrants on The Nasdaq Global Select Market or any other national securities exchange or nationally recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants will be limited.

We will not receive any additional funds upon the exercise of the pre-funded warrants.

Each pre-funded warrant will be exercisable from the date of issuance until such warrant is exercised in full and only by means of a cashless exercise, meaning that the holder would not pay a cash purchase price upon exercise, but instead would receive upon such exercise the net number of shares of our common stock determined according to the formula set forth in the pre-funded warrant. Accordingly, we will not receive any additional funds upon the exercise of the pre-funded warrants.

Except for the right to participate in certain dividends and distributions, holders of the pre-funded warrants will have no rights as common stockholders until such holders exercise their pre-funded warrants and acquire our common stock.

Until holders of the pre-funded warrants exercise their pre-funded warrants and acquire shares of our common stock, except for the right to participate in certain dividends and distributions, such holders will have no rights with respect to the shares of our common stock underlying such pre-funded warrants. Upon exercise of the pre-funded warrants, the holders will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

This offering is not contingent on the consummation of the concurrent private placement.

The consummation of the concurrent private placement is contingent on the closing of this offering and the satisfaction of certain other customary conditions. However, the consummation of this offering is not contingent on the consummation of the concurrent private placement. Accordingly,

if you decide to purchase shares of our common stock in this offering, you should be willing to do so whether or not we complete the concurrent private placement.

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 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 or other factors, including disruptions resulting from the COVID-19 pandemic, 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 commercializing pharmaceutical products. 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, funds we received under our prior Fovista licensing and commercialization agreement with Novartis Pharma AG, funds we received in connection with our acquisition of Inception 4 in October 2018, and our follow-on public offerings, which we closed in February 2014 and December 2019. As of March 31, 2020, we had an accumulated deficit of $495.6 million. Our net loss was $15.1 million for the three months ended March 31, 2020 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. We estimate that the aggregate external costs of our ISEE2008 Phase 3 clinical trial for Zimura in GA will range between $40.0 million and $45.0 million, and that the aggregate external costs associated with manufacturing process scale-up and validation for Zimura, as well as our costs to develop a second source manufacturer during the course of the ISEE2008 trial, will range between $30.0 million and $35.0 million. We also estimate that the aggregate external costs to expand the OPH2005 trial will be approximately $4.0 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. Furthermore, we expect that if the delay in initiating patient enrollment for the ISEE2008 trial becomes prolonged, whether due to the COVID-19 pandemic or other reasons, or if we experience additional delays or disruptions to our research and development programs, including in the manufacture and supply of products for such programs, such delays or disruptions could increase our operating expenses or otherwise have a material adverse effect on our business and financial results. 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., or Archemix, with respect to Zimura, the University of Florida Research Foundation, Incorporated, or 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 development of Zimura in GA and STGD1;

- 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;
- 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; 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 March 31, 2020, we had cash and cash equivalents of $108.4 million. 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. 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 current and planned Zimura clinical programs;
- the costs, progress, timing and results of process development, manufacturing scale-up and validation activities, analytical development and stability studies associated with Zimura and our other product candidates;
- 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 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 activities to establish manufacturing capabilities and formulation development and other preclinical development activities to enable us to file an IND for a product candidate from this program;
- the length of the delay to the initiation of the ISEE2008 trial and any other delays or disruptions to our research and development programs as a result of the COVID-19 pandemic;
- 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 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. For example, the COVID-19 pandemic has caused significant volatility and uncertainty in the financial markets as well as additional volatility in the price of our stock, which may result in prospective investors being less likely to invest new capital. 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. Although we were able to raise approximately $42.6 million in net proceeds through our December 2019 public offering, we may not be able to successfully raise additional capital. The size of our company and our status as a company listed on The Nasdaq Global Select 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 one or more 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 an issue in our clinical trials, such as issues with patient enrollment, the retention of enrolled patients, enrolled patients maintaining scheduled visits and receiving scheduled treatments, or the availability of drug supply, if we

experience an issue in our preclinical development programs, such as unfavorable toxicology or other preclinical data, inability to develop formulations or other issues with manufacturing, or if we modify or further expand the scope of our clinical trials, preclinical development programs or collaborative gene therapy sponsored research programs. For example, we have recently decided to enroll up to approximately 50 additional patients in our ongoing OPH2005 trial, with the goal of retaining 120 patients for 18-month analysis as was initially intended in the protocol for this trial, which will extend the duration of that trial and increase our costs of conducting that trial. Our costs may also exceed our expectations for other reasons, for example, if we are required by the FDA, the European Medicines Agency, or 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, build internal research capabilities or pursue internal research efforts. For example, we plan to begin the ISEE2008 trial, which is a single Phase 3 clinical trial evaluating Zimura for GA, with the expectation that data collected from such trial, if it is positive, together with data from our OPH2003 trial, will be sufficient to seek marketing approval in the United States and the European Union and we may subsequently decide to, or be required by regulatory authorities to, enroll additional patients in the ISEE2008 trial beyond our current expectations or conduct additional clinical trials for Zimura in GA in order to seek or maintain regulatory approval or qualify for reimbursement approval. In addition, in March 2020, we decided to delay the initiation of patient enrollment in the ISEE2008 trial because of the COVID-19 pandemic. The COVID-19 pandemic may result in additional delays to the initiation of the ISEE2008 trial or to our other research and development programs, which could cause us to continue to expend our cash resources while not progressing our research and development programs as expeditiously as we would have had the pandemic not occurred or persisted. Although we are planning to initiate patient enrollment in the ISEE2008 trial in June 2020, we may experience difficulty in enrolling or retaining patients or maintaining scheduled visits and treatments due to patients' fears of visiting clinical trial sites or ongoing restrictive measures requiring social distancing or limiting travel. 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 equity issuances 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 agreement and plan of merger pursuant to which we acquired Inception 4 and our HtrA1 inhibitor program, or the Inception 4 Merger Agreement, 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 UMass as partial upfront consideration for the in-license of our miniCEP290 program, and are obligated to issue up to 75,000 additional shares to UMass upon the achievement of a development milestone.

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. For example, if we choose to pursue a collaboration for Zimura, we may be required to relinquish certain valuable rights depending on the terms of such a transaction. 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.

The COVID-19 pandemic, which is a fluid and evolving situation, is negatively affecting our business and operations in a number of ways, including delaying the initiation of patient enrollment for our ISEE2008 trial, and its long-term effects are uncertain. In addition, the pandemic has caused substantial disruption in the financial markets and economies, which could adversely affect our business and operations.

In December 2019, an outbreak of respiratory illness caused by a novel coronavirus began in Wuhan, China. As of June 2020, that outbreak has led to at least eight million confirmed cases and at least 400,000 deaths worldwide, with most countries throughout the world confirming cases. The World Health Organization has declared the outbreak a global pandemic and the U.S. government and all 50 states have declared it to be a national or state emergency. In addition, a majority of the world's population has been affected by government efforts to slow the spread of the outbreak through stay-at-home and social distancing orders, shutdowns of businesses and public places, heightened border security, travel restrictions, quarantines and other measures. The outbreak and government measures taken in response have had a significant impact, both direct and indirect, on businesses and commerce, as a substantial number of people have been required to stay and work from home; worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical

services and supplies, has spiked, while demand for other goods and services, such as travel and conferences, has fallen.

The COVID-19 pandemic and measures taken to contain it have affected our business and operations in a number of ways. These include, but are not limited to, the following:

- In March 2020, we decided to delay initiation of patient enrollment in our ISEE2008 trial. In the meantime, we have continued with trial initiation activities and we plan to initiate patient enrollment in June 2020. Health authorities and ethics committees in certain countries, and many of the clinical trial sites we are planning to use for this trial, reduced their staff and operations due to the COVID-19 pandemic. This reduction in operations has resulted in delays to the approval of our trial in certain countries outside the United States and delays in the activation process for a number of our planned clinical trial sites. Although many clinical trial sites have started to reopen, many are doing so with reduced staff and operations and focusing on more urgent matters rather than clinical trials. We understand most sites are monitoring the COVID-19 situation closely and may reduce their operations if the COVID-19 pandemic persists or if there is a second wave. Although we have recently decided to initiate patient enrollment in the ISEE2008 trial, we may experience difficulty in enrolling or retaining patients due to patients' fears of visiting clinical trial sites, ongoing restrictive measures requiring social distancing or limiting travel or the reduced level of operations at many of our clinical trial sites.
- We instituted company-wide remote working starting in the middle of March 2020. Investor and scientific meetings and conferences have been canceled or are occurring virtually. We have been relying on remote means of working and communication both internally and externally.
- Many of our clinical trial sites for the OPH2003 and OPH2005 trials have been operating with reduced staff and other restrictions. We have increased our efforts to engage with our clinical trial sites with a focus on retaining patients and maintaining scheduled visits and treatments, and instituted practices such as flexible scheduling of visits for patients and remote monitoring. Based on the latest information we have available, we are aware that several patients in the OPH2005 trial have missed consecutive trial visits early on during the pandemic and the number of missed visits has recently been declining. We continue to monitor the situation closely. We do not yet know whether the trend in decreased missed visits will continue or reverse, or what the impact of these missed visits may be on the results of the trial, especially because we are masked to the treatment condition of these patients. We have recently decided to enroll up to approximately 50 additional patients in the OPH2005 trial, with the goal of retaining 120 patients for 18-month analysis as was initially intended in the protocol for the OPH2005 trial. We may experience difficulty in enrolling or retaining patients or maintaining scheduled visits and treatments in the future due to ongoing or future restrictions or other impacts related to the COVID-19 pandemic.
- In some instances, our third-party contract manufacturers, academic research collaborators and contract research organizations have limited their operations and staff, which has resulted in delays to some of our manufacturing and research and development activities and limited our ability to be on site to oversee these activities.
- Shortages and governmental restrictions arising from the COVID-19 pandemic may disrupt the ability of our contract manufacturers to procure items that are essential for our manufacturing activities, such as raw materials used in the manufacture of our product candidates. The manufacturer for our HtrA1 inhibitor program has experienced such a shortage. Our suppliers for certain vials used in the fill/finish services for our product candidates may allocate those vials for COVID-19 vaccines and medicines, which may reduce our ability to obtain those vials for our product candidates. Similar shortages and

governmental restrictions may disrupt our ability or the ability of our clinical trial sites to procure medical supplies for our clinical trials, including personal protective equipment to protect patients and investigators and their staffs.

- The pandemic has caused significant disruption to the financial markets, and has caused increased volatility in the price of our stock and that of other companies in the biotechnology industry.

We do not believe that the COVID-19 pandemic, and our actions in response and the costs of those actions, have had a material impact on our financial position, results of operations, or cash flows. However, the progression of the COVID-19 pandemic remains fluid and its impact on our business and operations remains uncertain. Even though the pandemic may be under control in several countries, there may be a second or subsequent waves as stay-at-home and social distancing orders are lifted. For example, in China, where the pandemic has been largely controlled since March 2020 and most of the country has reopened, there have been a number of recent cases resurfacing in Beijing, which has caused public health authorities to reimpose restrictive measures. The prospects for finding an effective vaccine or treatment for this disease are uncertain, which may cause the measures to contain the pandemic to be in place for a prolonged period of time. The full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition will depend on developments that are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning COVID-19, the actions taken to contain it or lessen its impact and the economic impact on local, regional, national and international markets. For example, if our clinical trial sites continue to have reduced operations or close, this could have a material adverse impact on our clinical trial plans and timelines. If the delays and other disruptions due to the pandemic become prolonged or more extensive, then we may experience further delays or disruptions to our research and development programs and our financial position, results of operations or cash flows for future periods may be materially affected.

In addition, many companies have been using force majeure clauses in their contracts to excuse or delay performing under their contracts. Our contract manufacturers, academic research collaborators, contract research organizations and other third parties on whom we rely for goods or services may make similar claims. If any such force majeure claims were successful, then not only would our timelines be delayed but also our right to recover for any economic damages due to the delay would be limited. Because we rely on many single-source suppliers, any such claims from them are likely to result in a delay to our timelines or otherwise adversely affect our operations or financial position.

We cannot foresee if and when the outbreak of COVID-19 will be effectively contained, nor can we predict the severity and duration of the impact of the pandemic on our operations. Currently, most of the new cases are located in the United States and Latin America, whereas most of Europe and Asia have seen reduced numbers of new cases. Even if the pandemic is contained and the economy is largely reopened, the pandemic may recur and the existing measures may be re-imposed. If the COVID-19 pandemic is not effectively and timely controlled, we may experience prolonged disruptions of our clinical trials, suppliers or contract manufacturers, extended closures of facilities, such as clinical trial sites, academic research centers and suppliers, including single source suppliers, and delays in interactions with regulatory agencies or approvals for our product candidates. Many economists are predicting that the pandemic may have significant or long-lasting effects on economies worldwide. If the effects of COVID-19 on the financial markets and the global economy persist, they could hamper our ability to raise additional finances. Any of these events may materially and adversely affect our business operations and financial condition.

Our strategy of obtaining additional rights to products, 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 as well as other compelling ophthalmology opportunities. Since early 2018, we have completed multiple acquisition, in-license, exclusive option and sponsored research arrangements for product candidates and other technologies intended to treat retinal diseases. We plan to continue to evaluate additional opportunities to in-license or acquire products, product candidates and technologies on a selective and targeted 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 development and potential commercialization of Zimura. Our business development efforts may fail to result in our acquiring rights to additional products, 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 products, 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. There are currently a limited number of available product candidates or technologies for the treatment of diseases affecting retina and the competition for those assets is intense. The process of proposing, negotiating and implementing a license or acquisition of a product candidate is lengthy and complex. With respect to potential product candidates or technologies for which we have entered into option agreements or sponsored research agreements for which we have option rights, our 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 options to acquire or in-license any product candidates or technologies.

The in-licensing and acquisition of pharmaceutical products 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. We believe that other companies may be particularly active in pursuing opportunities to in-license or acquire priming gene therapy opportunities. 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. The class action lawsuit is currently in the discovery phase. 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.

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, validating and receiving regulatory approval of our manufacturing processes and our third-party manufacturers' facilities and ensuring adequate supply of drug substance and drug product and starting materials used for the manufacture of drug substance and 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, including the IND-enabling toxicology studies we are conducting or planning to conduct for IC-100 and IC-200, 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 18-month results from our OPH2003 trial supported the 12-month results in this trial, at which time Zimura met the prespecified primary endpoint in reducing the mean rate of GA growth in patients with GA with statistical significance across both the Zimura 2 mg and Zimura 4 mg treatment groups when compared to the corresponding sham control groups with a favorable safety profile of Zimura, these results may not be replicated in the planned ISEE2008 trial or any other future trial we may conduct for Zimura in 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;
- 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 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 or quality of starting materials, such as plasmids used for the manufacture of our gene therapy product candidates and the polyethylene glycol used for the manufacture of Zimura, 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;
- we may not be able to successfully scale up or validate a manufacturing process for one or more of our product candidates, and may need to rely on second source suppliers for adequate supply of drug substance and/or drug product in line with our needs and expectations;
- 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, through our clinical trial sites, may not be able to maintain enrolled patients for scheduled visits and treatments, or to retain patients altogether, especially in light of the

COVID-19 pandemic, which could result in missing data from our clinical trials, potentially leading to uninterpretable results or a clinical trial not being sufficiently powered to demonstrate an efficacy benefit;

- 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 GA, Stargardt disease, RHO-adRP or Best disease, 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. The progress of our clinical trials may be dependent on macro-economic events beyond our control, such as the COVID-19 pandemic. For example, although we are planning to initiate patient enrollment in the ISEE2008 trial in June 2020, we may later decide to or be required to pause patient recruitment due to the continued persistence of the pandemic or if a second or subsequent wave of cases occurs. 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 AMD in a manner sufficient to support an application for regulatory approval to the FDA and EMA are based on our review of the 12-month data from the OPH2003 trial as well as informal discussions with the FDA. 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 have interactions with the FDA, as we continue to review and analyze data from our OPH2003 trial, including the recently available 18-month data, as we continue to plan for and as we conduct our ISEE2008 trial, 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, could 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 in GA and STGD1 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 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 GA secondary to AMD, and that the results from our OPH2003 trial of Zimura in GA support our view, this approach may not prove successful for treating GA secondary to AMD in a clinically meaningful way. Similarly, although there is non-clinical scientific literature supporting the potential use of complement system inhibitors 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 at month 12 and continued to show positive treatment effect at month 18, 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.

We are continuing to review and analyze the 18-month results and individual patient level data from the OPH2003 trial, which may affect the soundness of the conclusions we have drawn based on the results from this trial. The ISEE2008 trial may yield results that are different from the results observed in the OPH2003 trial.

Although the 18-month data from the OPH2003 trial supported the results we observed at 12 months, these data may be subject to several limitations. In accordance with the prespecified statistical analysis plan for the trial, we only performed descriptive analysis of the 18-month efficacy data, which limits our ability to draw meaningful conclusions from this data. Although the favorable safety profile for Zimura was maintained at month 18, we expect we will continue to analyze individual patient data on an unmasked basis, which will provide us a better understanding of the results and the variables affecting the results. These results may indicate that our 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. Additionally, we learned from our independent masked reading center that the retinal images of one of the patients showed evidence of CNV in the study eye that was not reported by the investigator. As we evaluate the individual patient data, we may learn of additional cases of non-investigator reported safety issues, which may affect the safety profile of Zimura.

Unlike the OPH2003 trial, the ISEE2008 trial will include only one treatment arm, Zimura 2 mg, in addition to a control arm. 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 study doses or treatment regimens within a single trial helps mitigate the risk of bias in the trial and is therefore recommended, although not required. 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 have decided to proceed with only one treatment arm in the ISEE2008 trial consisting of a single monthly administration of Zimura 2 mg, because the 12-month data from the OPH2003 trial suggested that monthly administration of Zimura 2 mg provides a similar benefit (approximately 27%) in reducing the mean rate of GA growth over 12 months as compared to the corresponding sham control group, as measured by our primary endpoint, as Zimura 4 mg, and these results are supported by the results of the 18-month data, and because we want to avoid the treatment burden associated with the Zimura 4 mg dose evaluated in our OPH2003 trial. Additionally, for our ISEE2008 trial, because we want to begin to evaluate the efficacy of a less frequent dosing regimen, we plan to re-randomize the patients in the monthly Zimura 2 mg treatment arm at 12 months and evaluate dosing Zimura 2 mg every other month, a dosing regimen which we have not previously studied, in half of those patients during the second 12 months of the trial. The ISEE2008 trial, however, is not designed to reliably assess any differences we observe between these treatment groups at 24 months with statistical significance and the label we would seek for Zimura in GA, if the results from the ISEE2008 trial are positive, would in all likelihood provide for monthly administration of Zimura.

We plan to conduct the ISEE2008 trial at many clinical trial sites that were not included in the OPH2003 trial. The introduction of new sites, and the resulting involvement of new treating physicians, as well as potentially different patient demographics, can introduce additional variability into the conduct of the trials in accordance with their protocols and may result in greater variability of patient outcomes, which could adversely affect our ability to detect statistically significant differences between patients treated with Zimura 2 mg and patients receiving sham control.

In addition, the 12-month and 18-month data from the OPH2003 trial suggested there is an overall dose response relationship in which higher doses of Zimura (for example, 4 mg dose) corresponded to a greater reduction in the mean rate of GA growth as compared to the corresponding sham group as compared to lower doses of Zimura (for example, 2 mg and 1 mg doses). For our ISEE2008 trial, for the reasons stated above, we have decided to proceed with only a 2 mg dose treatment arm and not include a 4 mg dose treatment arm. The 2 mg dose may prove not to be efficacious in treating GA. Additionally, unlike the protocol for the OPH2003 trial, the protocol of the ISEE2008 trial will provide that patients who develop CNV in the study eye in the trial may remain in the trial and receive standard of care anti-VEGF therapy, at the investigator's discretion, and that measurements of these patients' GA will be included in the primary efficacy analysis if their fundus autofluorescence, or FAF, images can be reliably assessed by the masked reading center. The retention of these patients in the ISEE2008 trial may introduce additional

variability not present in the OPH2003 trial. Moreover, if a significant number of patients develop CNV in the study eye and these patients' FAF images are not reliably assessable, or if more patients than we anticipate drop out or their data is otherwise missing, it would reduce the number of patients from whom data is available for analyzing the primary endpoint for this trial and the ISEE2008 trial could be underpowered to demonstrate a potential clinical benefit for Zimura in GA with statistical significance.

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 may be able to rely on the results from our OPH2003 trial as one of two well-controlled, Phase 3 trials typically required by the FDA. The FDA, EMA and other regulatory authorities may not accept the results of the OPH2003 trial as a Phase 3 clinical trial, or may not agree with our selection of the primary endpoint for the OPH2003 and ISEE2008 trials or the statistical analysis we performed. We may decide to or may be required to enroll additional patients, collect additional safety data or conduct additional clinical trials to seek or obtain approval for Zimura in GA.

Based on the results we have received from our OPH2003 trial, additional statistical analysis we have performed and 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 over 12 months 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. We are not currently planning to include visual function measures as primary or secondary efficacy endpoints in the ISEE2008 trial, and vision will be assessed as a safety endpoint. The FDA, the EMA or other regulatory authorities may disagree with our conclusion regarding the robustness of the data from the OPH2003 trial based on our sensitivity analyses or may conduct their own sensitivity analyses yielding different results. Even if we meet with the FDA, EMA or other regulatory authorities, 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, until such time as we submit an application for marketing 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 ISEE2008 trial, one or more additional, well-controlled clinical trials that meets the applicable regulatory requirements in order to obtain sufficiently robust data to support marketing 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 2 mg 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. We plan to use the same MRM analysis in the ISEE2008 trial. 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 the clinical data set from our OPH2003 trial, 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 informal discussions with the FDA, we believe we need to conduct one additional clinical trial with enough patients such that we will have safety data for a minimum of 300 patients having received the dose of Zimura for which we are seeking approval, or a higher Zimura dose, independent of indication, for a minimum of 12 months, with 24-month safety data available for some portion, but not all, of these 300 patients. This additional clinical trial would need to be well-controlled, with a primary efficacy analysis at the 12 month time point or later. We believe that if we were to file an application for marketing approval for Zimura for GA, we would be able to rely on safety data from our OPH2003 and ISEE2008 trials in GA, as well as our OPH2005 trial evaluating Zimura for STGD1. We also believe that, if the data from the ISEE2008 trial are positive, we would be able to submit our application following the primary efficacy analysis for the ISEE2008 study at the 12-month time point, without waiting for the full 24-month data package, that we could continue collecting data after submitting for marketing approval and that we could supplement our applications for marketing approval while they are pending. We have designed our ISEE2008 trial to meet these requirements, which, as we understand them, and if data from the ISEE2008 trial are positive, will permit us to seek marketing approval for Zimura in GA in the United States and potentially the European Union. We have not had formal interactions with either the FDA or the EMA regarding the ISEE2008 trial and may not do so before receiving results from the trial and submitting our applications for marketing approval. In addition, we expect to engage with regulatory authorities, including with the FDA as part of the fast track program or otherwise with competent national authorities in Europe, during the trial and may receive feedback that is not consistent with our expectations, including potential disagreements by the EMA and other regulatory authorities with what we are understand are the requirements of the FDA. Regulatory authorities may require us to enroll additional patients, collect additional safety data, conduct additional trials or take other actions, which would require us to revise our development plans for Zimura, including potentially changing the design of the ISEE2008 trial, increase the costs of our Zimura clinical programs and delay our expected timelines. In addition, because of the COVID-19 pandemic or other reasons, after we initiate the trial, we may experience a higher than anticipated rate of dropouts and missed visits and treatments in our ISEE2008 trial, which could result in our not having adequate safety data for a sufficient number of patients, even if the primary endpoint is met and the results from the ISEE2008 are otherwise positive.

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 have not observed any adverse events or serious adverse events attributable by the investigators to the drug product in our OPH2003 trial,

we may become aware of safety concerns as we analyze individual patient level data in our OPH2003 trial, and they may manifest in our OPH2005 trial, in our planned ISEE2008 trial or in any other 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 observe safety events 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.*"

Because the primary efficacy endpoint and the statistical analysis plan we would expect to use to analyze data for the primary efficacy endpoint for our ISEE2008 trial are similar to those of the OPH2003 trial, any disagreements by the FDA, EMA or other regulatory authorities with OPH2003 will likely affect ISEE2008 as well. Our ongoing and planned clinical trials and any other 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 planned or any other future clinical trials for Zimura could adversely affect our business and the value of your investment in our company.

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

We have no unmasked 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 during the second half 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 other forms of AMD, may not perceive a benefit from continuing to participate and therefore may drop out of this trial or miss scheduled visits and treatments. This risk is particularly magnified during the COVID-19 pandemic, which may cause our patients to voluntarily or involuntarily drop out of the trial or miss scheduled visits and treatments in greater numbers than before. Although we and the investigators and their staff take efforts to encourage continued patient participation, the dropout rate may exceed our expectations. A higher than expected dropout 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.

Based on the latest available data from the OPH2005 trial, although there have been increased patient dropouts and missed visits over the course of the COVID-19 pandemic, we do not believe they are significantly higher than expected. We have decided to enroll up to approximately 50 additional patients in this trial, with the goal of retaining 120 patients for 18 month analysis as was initially intended in the protocol for this trial. This change to the trial will increase the costs associated with this trial and delay the timelines for receipt of data from this trial. We believe an

expanded trial could allow us to collect additional data regarding the effect of Zimura on STGD1 patients and help us mitigate the risks from additional patient dropouts and missed visits; however, these expectations may prove to be incorrect.

The COVID-19 pandemic has affected and may continue to affect the initiation and conduct of our clinical trials, including the timing and progress of trial initiation activities for ISEE2008 and the retention of patients for our clinical trials. It may have long-lasting effects on the conduct of trials for the treatment of GA, which can make future trials more difficult or time consuming.

Our OPH2003, OPH2005 and ISEE2008 trials involve sites located across the United States and in many countries outside the United States. We have made a number of changes to the clinical operations of our ongoing and planned trials as a result of the COVID-19 pandemic, its effects on current and prospective participating patients, and various governmental and other measures to control the outbreak. Our plans for our clinical trials may change further as the COVID-19 situation evolves.

For our OPH2003 trial, the outbreak proliferated around the world as we were finishing the final visits for patients in this trial. In addition to the disruptions to the operations of many clinical trial sites, the COVID-19 pandemic has affected our monitoring operations, for example, by requiring remote monitoring and remote source document verification in many instances, which may affect the robustness of the data verification process, which we may find out as we evaluate the unmasked individual patient level data from this trial.

For our OPH2005 trial, as of June 15, 2020, 36 patients remain active and the final patient visits are not expected to occur until the second half of this year. As with OPH2003, we have focused our efforts on maintaining scheduled visits and treatments and overall patient retention. As compared to the patients in the OPH2003 trial, the patients in the OPH2005 trial are generally younger and have work and family commitments, which may cause them to miss more visits or drop out in greater numbers as a result of the COVID-19 pandemic. In addition to the risks posed by increased patient dropouts, if patients miss scheduled visits in greater numbers as a result of the pandemic, it may affect our ability to draw meaningful conclusions from the clinical data. We have provided additional flexibility for patients to modify the scheduling of their visits. To date, we have not seen a significant number of patient dropouts or missed visits attributable to the COVID-19 pandemic. However, especially if the COVID-19 pandemic persists, additional patient visits may be missed or rescheduled, which may delay the availability of top-line data from this trial and affect the interpretability of the data that we collect and the conclusions we are able to draw from these data.

For our ISEE2008 trial, in addition to the delay of patient enrollment, competent health authorities and ethics committees in certain countries and many clinical trial sites have reduced their staff and operations due to COVID-19. The reduction in operations has resulted in delays to the approval of our trial and the site activation process in certain geographies. Although we are planning to initiate patient enrollment in June 2020, our ability to activate clinical sites and to start our trial as planned will depend on the local situation in each specific geography.

We believe the COVID-19 pandemic and its effects will continue to affect patient recruitment, maintenance of scheduled visits and treatments and overall retention of patients in clinical trials, especially GA trials. As a result of the pandemic, many clinical trial sites may have limited capability to recruit patients, especially in a short period of time. Patients, in turn, may be reluctant to enroll in clinical trials or to maintain their scheduled visits and treatments once enrolled due to their fears of visiting clinical trial sites or ongoing restrictive measures requiring social distancing or limiting travel.

These concerns may particularly apply to GA patients, many of whom are elderly and therefore at a higher risk for COVID-19 and other diseases than the general population. In addition, many of the tests involved in GA trials, such as the retina imaging tests, are time consuming and may be onerous for patients. These factors may make patient recruitment and maintenance of scheduled visits for future clinical trials, especially GA trials, more difficult. Even if a site successfully enrolls patients in line with expectations, there may be additional patient dropouts or missed visits due to the COVID-19 pandemic or similar events, and if those events occur during the course of the ISEE2008 trial, they will likely affect our ability to complete this trial and obtain data in accordance with our expectations. Furthermore, because we expect the ISEE2008 trial to be ongoing for at least 24 months, which is the length of the trial, plus any additional time for patient recruitment, it is likely to be affected to the extent a second wave or subsequent outbreaks of the COVID-19 pandemic cause disruptions. Many clinical trial sites have changed their practices in preparation for a possible second wave or future outbreaks, and these changes may affect how we conduct the ISEE2008 trial, the expanded OPH2005 trial and any other future clinical trials we may conduct.

Gene therapy is an emerging field of drug development that poses many scientific and other risks. As a company, 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 and the limited patient populations for our gene therapy programs 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, especially if the mutation is associated with the production of a toxic protein. 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 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.

We have not previously conducted any clinical development involving gene therapies. As we prepare for the potential initiation of our first gene therapy clinical trial, we will need to build our internal and external capabilities in designing and executing a gene therapy clinical trial. There are many known and unknown risks involved in translating preclinical development of gene therapies to clinical development, including selecting appropriate endpoints and dosage levels for dosing humans based on preclinical data. Furthermore, our gene therapy programs are targeting orphan diseases with relatively small populations, which limits the pool of potential subjects for our gene therapy clinical trials. Because gene therapy trials generally require subjects who have not previously received any other therapy for the same indication, we will also need to compete with our competitors who are also developing therapies for these same indications for the same group of potential clinical trial subjects. If we are unable to initiate and conduct our gene therapy clinical trials in a manner that satisfies our expectations or regulatory requirements, the value of our gene therapy programs may be diminished.

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 selected lead compound in this program to determine whether we can identify a viable manufacturing process for and formulate the lead compound 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 our lead compound or any backup compound 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 costly and 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.

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 unmasked 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 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. Although the safety profile of Zimura remained favorable at month 18 in our OPH2003 trial, we may encounter unknown safety issues as we analyze the unmasked individual patient level data. An unforeseen or unexpected safety event, or any safety finding that is inconsistent with our prior experience with Zimura, from any of our clinical trials for Zimura, including from the ISEE2008 trial during which we will follow patients and collect safety data over 24 months, 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 retinal 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, one or more retinal surgeons must repeat the same subretinal injection process in multiple patients with consistency across patients and surgeons. 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. We identified an issue with one of the starting materials used to manufacture our IC-100 product candidate, which has delayed our timelines for that program, and we may encounter other manufacturing issues that could cause further 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. If any of our product candidates is approved, a manufacturing issue could result in product shortages, which could impair our ability to commercialize our products and generate revenue.

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. The manufacturing processes for our product candidates are technically complex. Problems with developing, executing or scaling up 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, insufficient inventory or delays in our programs. 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. None of our third-party manufacturers have undergone a pre-approval inspection by the FDA for Zimura or any of our other product candidates. 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 collaborations, 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, including the effects of the COVID-19 pandemic on our 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. As we plan for and conduct our ISEE2008 trial, we and our third-party manufacturers will need to complete several activities to ensure the continued supply of drug product for the trial and adequate preparations to support potential future commercial supply of Zimura. Any delay or failure in completing these activities could cause delays for the development of Zimura or its potential approval or could result in inadequate commercial product supply.

We currently use a single third-party manufacturer, Agilent, to supply us with the chemically synthesized drug substance for Zimura and a different, single third-party manufacturer, Ajinomoto, to provide fill/finish services for Zimura. We obtain the PEG reagent used to make Zimura drug substance from a single third-party manufacturer. In order to obtain and maintain regulatory approval for Zimura, our third-party manufacturers will be required to produce the Zimura drug substance with consistent quality and to execute fill/finish services on a repeated basis and document their ability to do so. In order for us to successfully commercialize Zimura, if approved, our manufacturers also need to be able to produce quantities at a commercial scale. If our third-party manufacturers are unable to satisfy these requirements, our business would be materially and adversely affected. 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.

In early 2017, we completed the small scale manufacture of multiple batches of Zimura API that we plan to use to support clinical drug supply for the ISEE2008 trial and the expanded OPH2005 trial. Although we believe we have adequate Zimura API for the ISEE2008 trial and the expanded OPH2005 trial, this supply may not be sufficient for our needs over the duration of the trials. We are

in discussions with our contract manufacturer about recommencing manufacturing activities, with the goal of scaling up and validating the manufacturing process to support the potential commercialization of Zimura. We are also planning to engage a different manufacturer for the Zimura API. We will need to demonstrate that Zimura API produced through the scaled-up process is analytically comparable to the Zimura we are currently using before API manufactured through the scaled-up process can be used for commercial drug supply. In addition, we are in the process of securing remaining finished drug product sufficient to support the needs for the ISEE2008 trial and the expanded OPH2005 trial. We plan to make a change to the vial currently used for the finished Zimura drug product to support a more robust fill/finish operation at commercial scale. We have also engaged a second source supplier to support us with additional clinical supply of the finished Zimura drug product. Each of these activities is costly, time-consuming and uncertain in outcome. We may not be able to successfully scale up or validate our manufacturing process for Zimura, demonstrate analytical comparability of the Zimura API manufactured through the scaled up process with the previously manufactured Zimura API, or establish the long-term stability of the finished Zimura drug product stored in the new vial container. The new manufacturers we have or are planning to engage have not had previous experience with Zimura and there may be issues with technology transfer. We may need to perform additional work beyond what we currently plan to establish manufacturing and analytical capabilities sufficient to obtain regulatory approval of our manufacturing process for Zimura and to support potential commercial operations. If any of the foregoing events occur, it could result in delays or increased costs to support our future development and commercialization of Zimura, even if we successfully complete any required clinical trials for Zimura and obtain sufficient and favorable safety and efficacy data.

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.

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, including during process development and cGMP manufacturing, may result in unanticipated delays to our timelines, including delays attributable to securing additional manufacturing time 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.

For IC-100, we identified an issue with one of the starting materials used for our manufacturing process. That issue caused us to delay our cGMP manufacturing run at our CDMO, and we had to reschedule the run for a later date based on the CDMO's availability. The supplier has since provided new starting materials for our rescheduled cGMP manufacturing run. If there are issues with the new starting materials, the success of the manufacturing campaign and our timelines and the future development of IC-100 could be adversely affected.

A number of factors common to the manufacturing of biologics and drugs could also cause production or quality issues for gene therapies, including raw material or starting material variability in terms of quality, cell line viability, productivity or stability issues, product and process impurities, 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, epidemics and pandemics, 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, for IC-100 and IC-200 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 and analytical methods. 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.

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.

An important part of manufacturing drug products is performing analytical testing. Analytical testing of gene therapies involves tests that are more complex in scope and take a longer time to develop and to conduct as compared to those used for 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 or applicable requirements, we may need to delay or repeat certain manufacturing and development activities.

We are only in the early stages of establishing manufacturing capabilities for our HtrA1 inhibitor program.

We have engaged a CDMO to conduct process development, scale-up and cGMP manufacture of the API for the lead compound from our HtrA1 inhibitor program 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.

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 a business strategy that includes 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 or less frequent method of administration, however, might have a competitive advantage over one administered by monthly intravitreal injections, 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 would 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 GA or dry AMD:

- There are a number of products in preclinical and clinical development by third parties to treat GA or 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., or Apellis, Roche AG, Novartis AG and MorphoSys AG, Hemera Biosciences, Inc., Gemini Therapeutics, Inc., NGM Biopharmaceuticals Inc., Gyroscope Therapeutics, Achillion Pharmaceuticals, Inc., and Biogen Inc. each have complement inhibitors in development for GA or 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 April 2020, Apellis confirmed its expectation that it would finish patient enrollment in its Phase 3 program by the end of the first half of 2020 with the goal of enrolling approximately 1,200 patients, and it would announce data from the trials in the third quarter 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 Allergan Inc., Allegro Ophthalmics, LLC, Alkeus Pharmaceuticals Inc., EyePoint Pharmaceuticals, Inc., Lineage Cell Therapeutics, Inc., Roche AG and Stealth BioTherapeutics Corp. (working in collaboration with Alexion Pharmaceuticals, Inc.), are pursuing development programs for the treatment GA or dry AMD using 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 Inc.), 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. Sanofi 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, Inc. (in partnership with Allergan plc) has a 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 or dedicated personnel. 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 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 to or by a subgroup of patients, including, for example, for Zimura, if approved, restrictions on use of our product to patients with GA secondary to dry AMD (as opposed to GA secondary to any or all forms of AMD) or to patients with specific GA lesion characteristics, such as non-foveal GA, or 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 frequent dosing regimen than monthly intravitreal injections, in the case of Zimura, or a less invasive method of administration than subretinal injection, in the case of our gene therapy product candidates, come to market. For example, Apellis is testing its complement inhibitor product candidate for GA with both monthly and every other month dosing regimens, and may obtain a label with an every other month dosing regimen with similar efficacy as the monthly dosing regimen, while we expect that any label we may obtain for Zimura in GA will require monthly administrations. If so, physicians and patients may find Apellis's dosing regimen more convenient than ours.

Our development program for Zimura in GA uses an anatomical primary endpoint, the mean rate of change in GA growth over 12 months. 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 corollary to the anatomical measure that we are using as our primary endpoint. Although we evaluated visual acuity as a secondary endpoint in the OPH2003 trial, the trial was not designed to reliably assess differences in mean changes in visual acuity with statistical significance. Patients, physicians and payors may not recognize the value of, and we may not be able to obtain marketing or reimbursement approval for, Zimura without demonstrating a functional benefit to vision. To do so, we may need to conduct additional clinical trials, which may not ultimately demonstrate a functional benefit to vision.

For each of our Zimura trials where patients receive multiple intravitreal injections on the same day, including the OPH2005 trial, 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, including for example, for autosomal recessive Stargardt disease, 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.

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 is a variety of factors that could contribute to the actual number of patients who receive an approved therapy being less than our estimates of the potential 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. The number of patients in the United States, the European Union and elsewhere may turn out to be lower than expected, patients may not be amenable to treatment with our products or patients may become increasingly difficult to identify and access, all of which would adversely affect our business, financial condition, results of operations and prospects. 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, both of which launched in the United States within the past two years, 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 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, the U.S. Congress 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. The reference pricing model has found support from some members of the U.S. Congress. 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, which President Trump and many members of the U.S. Congress expressed an interest in pursuing. In December 2019, the Department of Health and Human Services proposed a rule permitting limited importation of drugs from Canada. 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 or in-license. 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 candidates of sufficient quality, which could delay, prevent or impair our development or commercialization efforts. The COVID-19 pandemic has affected our contract manufacturers' operations and the manufacture of our product candidates.

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. We do not currently have any contractual commitments for the supply of Zimura drug substance with this manufacturer and we may not be able to come to agreement with this manufacturer for scale up and validation activities and long-term clinical or commercial supply. We are planning to engage a different manufacturer for additional supply of drug substance for Zimura. We have recently engaged a second supplier for the 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 conduct process development, scale-up and cGMP manufacture of the API of our lead compound 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.

As a result of the COVID-19 pandemic, our third-party contract manufacturers and many sole-source suppliers have limited their operations by reducing the number of staff on site and instituting restrictions on visitors. These changes may result in delays to the progress of our manufacturing activities or affect their quality. For example, we have not been able to perform

person-in-plant (PIP) observations on a number of critical manufacturing activities at our CDMO for IC-100 and IC-200, which may affect the quality of the materials produced during those activities. Additionally, shortages and governmental restrictions arising from the COVID-19 pandemic may disrupt the ability of our contract manufacturers to procure items that are essential for our manufacturing activities, such as raw materials used in the manufacture of our product candidates. For example, our contract manufacturer for our HtrA1 inhibitor program experienced shortages in one of the raw materials that was sourced from China, which was affected by the slowdown in trade due to the COVID-19 pandemic.

Our third-party manufacturer for the API for Zimura and our CDMO for IC-100 and IC-200 are currently undergoing rapid expansion, including ramping up for production for existing clients, bringing on additional clients, opening new facilities, installing and validating new equipment, and hiring and training new personnel. Our third-party manufacturer for Zimura API informed us that as a result of competing demands from other customers, its ability to support our scale up and future manufacturing activities for Zimura is limited. As a result, we may be required to use a different supplier that may become our primary or new sole supplier for Zimura API, and the timing, costs, progress, quality and outcome of our planned manufacturing activities for Zimura may be negatively affected. In addition, expansion experienced by other manufacturers and suppliers that we use, including any issues that they may experience while expanding, could negatively impact the timing, costs, progress, quality and outcome of our planned manufacturing activities with those manufacturers and delay or hinder our development plans.

If any of our third-party manufacturers, fill/finish providers or sole-source suppliers fail to fulfill our contracts or 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, we and our third party manufacturers source some of the raw and starting materials used in the manufacture of our product candidates from 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. The COVID-19 pandemic and governmental measures in response may also cause delays or disruptions to our supply of starting materials.

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. The COVID-19 pandemic has affected operations at our academic collaborators and our sponsored research 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. These third parties may also have relationships with other entities, some of which may be our competitors. 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.

We also rely upon our university collaborators to conduct some of our preclinical studies. In particular, Penn has the canine disease model for two of the diseases we are aiming to treat: RHO-adRP and *BEST1*-related retinal diseases. Our preclinical development plans for both IC-100 and IC-200 include conducting certain preclinical studies using the associated canine disease models. If the canines that we are intending to use are not available to us for any reason, our development of IC-100 or IC-200 could potentially be delayed or otherwise adversely affected.

The COVID-19 pandemic has caused our university collaborators to limit the number of staff on site and the types of activities that may be conducted in their laboratories. Penn has restricted their researchers from being on site in their laboratories and closed a number of research centers that our researchers use for data analysis, which has limited their ability to analyze some of the data generated during our preclinical studies. As a result, our receipt of data and reports from those studies may be delayed or we may be required to curtail some of the analysis we had originally planned. The University of Florida, or UF, has also limited staff on site in their laboratories and vector production facilities, which has delayed our obtaining certain reagents and other materials used for our gene therapy programs. In addition, UMMS has suspended researcher access to their laboratories and the conduct of certain animal studies, which has delayed our timelines for our miniCEP290 program and may also delay our receipt of results from our miniABCA4 and miniUSH2A sponsored research programs. Shortages and governmental restrictions arising from the COVID-19 pandemic may also disrupt the ability of our academic collaborators, clinical trial sites and other contract research organizations to procure items that are essential for our research and development activities, including, for example, medical and laboratory supplies used in our clinical trials or preclinical studies or animals that are used for preclinical studies. There is no guarantee that the COVID-19 pandemic will not further impact our supply chain, which could have a material impact on our research and development programs.

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 and other regulatory authorities require 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 various government-sponsored databases within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Over the past few years, there has been increasing oversight by the FDA and other regulatory authorities on data integrity, especially in the research and development of novel therapies such as gene therapies. We rely upon the practices of and systems in place at our third party collaborators in generating data to support our preclinical and clinical development programs and for quality control over this data. Their practices and systems vary in scope and effectiveness and we have a limited number of personnel to supervise, including to perform quality assurance of, those practices and systems. 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. 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.

We also rely upon other third parties to store, package, label and distribute drug supplies for our clinical trials and to store materials for our development activities. In particular, we rely on a limited number of third parties to store starting materials, drug substance and drug product for our product candidates and programs. 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 continue to explore potential 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 our gene therapy programs, 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 with marketing and distribution rights to one or more of our products may not commit sufficient resources to the marketing and distribution of such product or products;
- 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;
- laws or practices in certain foreign jurisdictions may require that as a condition of working with a collaborator in such jurisdiction, we agree to certain foreign ownership restrictions, use certain local services or providers, share or license certain of our proprietary information or technology or other conditions that are not attractive to us; 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 $5.0 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, IC-200, 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.

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.

Our licensed patent rights for IC-200 and certain of our licensed patent rights for Zimura and IC-100 are method-of-treatment patents and patent applications. 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 our product candidates would limit our ability to generate revenue from the sale of such 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 IC-100 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 IC-100 in that jurisdiction so long as these competitors do not infringe any of our other patents covering Zimura's or IC-100'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 or IC-100, even if such use infringes any of our method-of-treatment patents.

Additionally, we do not currently have any composition-of-matter patent applications or patents covering IC-200. The method-of-treatment patent applications that Penn filed and which we in-licensed may be declared unpatentable or invalidated. If the patent applications protecting IC-200 are declared unpatentable or invalidated, it may diminish the value of IC-200 and our competitive position.

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.

The COVID-19 pandemic has caused the USPTO and many foreign patent offices to adjust their filing deadlines and requirements for applicants. While some of those changes may be beneficial to us, there is added uncertainty with regard to many procedural requirements, which may result in inadvertent non-compliance with those requirements that result in abandonment or lapse of patent rights. Additionally, the reduced staff and operations at many patent offices may delay the prosecution of patent rights or limit us or our patent agents' ability to interact with them.

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 and Data Protection

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. Information technology risks have become more significant over time, including as a result of widespread remote working during the COVID-19 pandemic.

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, including social engineering training, for our employees and consultants with access to our information technology systems and engagement of a third-party vendor to regularly 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.

In particular, as a result of the COVID-19 pandemic, we have switched to remote working since mid-March 2020 and as a result, have increasingly relied upon teleconferencing and cloud-based means of communication. Many other companies have done the same. There have been numerous publicized attempts of bad actors attempting to intercept proprietary communications. We may be similarly susceptible to those kinds of threats.

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, and those frameworks may not be consistent. 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 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. The GDPR also provides certain discretion to individual European member states, and many of them have enacted local legislation that differ from one another. We are aware that many other countries have enacted or are considering legislation similar to the GDPR.

Similar actions are either in place or under way in the United States. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels with the authority to review our privacy and data security practices based on general consumer protection laws. The Federal Trade Commission and state Attorneys General have been increasingly active in reviewing companies' privacy and data security practices in relation to consumer information. New legislation and regulations are also being

considered at both the state and federal levels. For example, the California Consumer Privacy Act, or the CCPA, which went into effect on January 1, 2020, is creating similar risks and obligations as those created by GDPR, although the CCPA exempts certain information collected as part of a clinical trial that is subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. We also may be subject to consumer class action litigation related to alleged noncompliance with these laws. Even if we are not determined to have violated these laws, responding to government investigations and/or consumer litigation in these areas typically requires the expenditure of significant resources and has the potential to generate negative publicity, which could harm our reputation and our business.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with these 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. 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, has resulted in certain changes to our business practices, such as additional consideration to the GDPR in setting up clinical trial agreements and informed consent forms for our ISEE2008 trial, and may require further changes to our business practices. Any non-compliance by us or our employees, consultants or contractors with the GDPR or other data protection laws could lead to setbacks in the development or approval of our product candidates, 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.

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.

In June 2016, the electorate in the United Kingdom, or UK, voted in favor of leaving the European Union, commonly referred to as "Brexit". Following protracted negotiations, the UK left the European Union on January 31, 2020. There is a transitional period until December 31, 2020, and the UK government and the European Union are attempting to agree to long-term trade and other agreements. Since the existing regulatory framework for pharmaceutical products in the UK is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime for pharmaceutical products in the UK, which remains uncertain. 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.

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.

In April 2020, the FDA granted fast track designation to Zimura for the treatment of GA secondary to dry AMD. Even though Zimura has received fast track designation, we must continue to follow the requirements of the program in order to maintain the fast track designation, and even if we maintain the designation, we may not ultimately experience a faster development process, review or approval compared to conventional FDA procedures. The FDA's grant of fast track designation to Zimura for the treatment of GA secondary to dry AMD does not imply that the FDA will grant fast track designation to Zimura for another indication, such as STGD1, or that the FDA will grant fast track designation for any of our other product candidates, if we choose to apply for fast track designation.

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 remains in flux in the context of gene therapies, and the FDA has issued recent draft guidance suggesting that it would not consider two gene therapy products to be different drugs solely based on minor differences in the transgenes or vectors. 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 $11,181 and a maximum of $22,363 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, imprisonment, 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.

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 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 TCJA, 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 led 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 led 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 $12.0 billion in ACA risk corridor payments to third-party payors who argued the payments were owed to them, a decision which the U.S. Supreme Court reversed on April 27, 2020. 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. Additional executive actions or regulations may be forthcoming.

In addition, in December 2018, a U.S. District Court in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the

ACA are invalid as well. The Trump Administration and CMS have both stated that the ruling will have no immediate effect, and later in December 2018, the same court issued an order staying the judgment pending appeal. In December 2019, the U.S. Circuit Court of Appeals for the Fifth Circuit affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. In March 2020, the U.S. Supreme Court agreed to review this decision, which will likely be in its next term. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

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. For example, in December 2019, the Trump Administration published proposed rules that, if finalized, would allow states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants would be required to demonstrate their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. At the same time, the FDA issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

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.

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. Additionally, the COVID-19 pandemic has caused many regulatory agencies, including the FDA, to reduce staff availability and operations. In addition, we may face impediments to scheduling or conducting regulatory meetings and approvals due to measures intended to limit in-person interactions. If a prolonged government restriction or 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.

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 and consultants.

We are a development-stage company with a total of 46 full-time employees as of June 1, 2020. These employees support key areas of our business and operations, including clinical operations, regulatory affairs, drug safety, data management, medical affairs, scientific research, 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 or become unavailable due to the COVID-19 pandemic or other reasons, 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. In preparation for our ISEE2008 trial and future development and potential commercialization of Zimura, we expect we will need to hire additional clinical operations, manufacturing, medical, regulatory and other personnel from this limited pool. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. The COVID-19 pandemic has made interviewing and hiring qualified candidates more difficult.

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.

As a result of the COVID-19 pandemic, our entire company has been working remotely since March 2020 and we expect to continue working remotely in the near future. Our ability to work remotely and transition effectively to working in our offices may affect our operations and the success of our company going forward.

In the middle of March 2020, we instituted a company-wide working from home policy, which has remained in effect. Our working from home policy may negatively impact productivity or disrupt our business, the magnitude of which will depend, in part, on the length of this remote working arrangement and other limitations on our ability to conduct our business in the ordinary course. We expect to work from home in the near future and will closely follow the guidance from federal and state authorities, including the Centers for Disease Control and Prevention, the New York State Department of Health and the New Jersey Department of Health, in deciding when to transition back to working in our offices. We expect the transition to occur in stages. When we transition back to working at company sites, there may be an increased risk to our employees and contractors, including as a result of a second or subsequent wave of the COVID-19 pandemic. Because of our small size and the importance of our employees and contractors to the success of our company, their exposure to the COVID-19 pandemic may adversely affect our ability to carry on our operations.

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 2015 our management concluded that we experienced a material weakness in internal controls that required us to restate the relevant financial statements and we took steps that year to address the deficiency and prevent similar deficiencies in the future. 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 the decrease in staffing in our accounting and finance areas following our reduction in force during 2017, will ensure that we maintain adequate controls over our financial reporting going forward and, accordingly, additional material weaknesses could occur or be identified. The COVID-19 pandemic may also affect the effectiveness of our internal controls. 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, such as those caused by the COVID-19 pandemic;
- political, regulatory or legal developments in the United States and other countries; and
- the other factors described in this "Risk Factors" section.

In addition, the COVID-19 pandemic has caused significant disruptions in the financial markets, and may continue to cause such disruptions, and has also impacted, and may continue to impact, the volatility of our stock price and trading in our stock. 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 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.

The ownership percentage of our stockholders may be diluted in the future, which could dilute the voting power or reduce the value of our outstanding shares of common stock.

As with any publicly traded company, the ownership percentage of our stockholders may be diluted in the future because of equity issuances for acquisitions, capital markets transactions, business development transactions or otherwise, including equity awards that we intend to continue to grant to our directors, officers and employees pursuant to our equity compensation plans. Our employees are also entitled, subject to certain conditions, to purchase our ordinary shares at a discount pursuant to our Employee Stock Purchase Plan.

In addition, the warrants that we issued in connection with our December 2019 public offering are exercisable at any time, and any exercise of such warrants will increase the number of shares of our outstanding common stock, which may dilute the ownership percentage or voting power of our stockholders.

Also, our certificate of incorporation authorizes us to issue, without the approval of our shareholders, one or more classes or series of preferred stock having such designation, powers, preferences and relative, participating, optional and other special rights, including preferences over our common stock with respect to dividends and distributions, as our board of directors generally may determine. The terms of one or more classes or series of preferred stock could dilute the voting power or reduce the value of our ordinary shares. Similarly, the repurchase or redemption rights or liquidation preferences we could assign to holders of preferred stock could affect the residual value of our common stock.

For more information about the dilutive effects of financing or business development transactions we may undertake, see the risk factor above, "*Raising additional capital may cause*

dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates."

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.

USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of shares of our common stock and pre-funded warrants in this offering will be approximately $ million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise in full their option to purchase additional shares, we estimate that the net proceeds from this offering will be approximately $ million. We will not receive any additional proceeds from the exercise of pre-funded warrants.

We estimate that the net proceeds from the concurrent private placement will be approximately $ million, after deducting placement agent fees and estimated offering expenses payable by us.

We plan to use the net proceeds from this offering and the concurrent private placement to fund clinical development of, and to further develop our manufacturing capabilities for, Zimura, to fund preclinical research and development and potential clinical development of our gene therapy portfolio and HtrA1 inhibitor program, and for working capital and other general corporate purposes.

We estimate that the aggregate external costs of our ISEE2008 Phase 3 clinical trial for Zimura in GA will range between $40.0 million and $45.0 million, and that the aggregate external costs associated with manufacturing process scale-up and validation for Zimura, as well as our costs to develop a second source manufacturer during the course of the ISEE2008 trial, will range between $30.0 million and $35.0 million. We also estimate that the aggregate external costs to expand the OPH2005 clinical trial will be approximately $4.0 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.

This expected use of the net proceeds from this offering and the concurrent private placement represents our intentions based upon our current plans and business conditions. We have not determined the exact amounts we plan to spend on any of the items listed above or the timing of these expenditures. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the actual net proceeds from this offering and the concurrent private placement, the progress of our development efforts, the status of and results from clinical trials and other research and development activities, as well as any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering and the concurrent private placement.

As of March 31, 2020, we had cash and cash equivalents of approximately $108.4 million.

Based upon our current operating plan, we estimate that the net proceeds from this offering and the concurrent private placement, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements as currently planned at least through the end of 2022. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. See the "Risk Factors" section of this prospectus supplement and the documents incorporated by reference for a discussion of the risks affecting our business that could have an adverse effect on our available capital resources.

We may also use a portion of the net proceeds from this offering and the concurrent private placement for the acquisition or in-license of additional products, product candidates, businesses or technologies, and the research, development and potential commercialization of the same, although we do not currently have any agreements or commitments for any future material acquisition or license of any such additional products, product candidates, businesses or technologies. Pending application of the net proceeds as described above, we may temporarily invest the net proceeds in a variety of capital preservation instruments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization as of March 31, 2020, as follows:

- on an actual basis; and
- on an as adjusted basis to give effect to our issuance and sale of (i) $ million of shares of our common stock and pre-funded warrants in this offering at a public offering price of $ per share of common stock and $ per pre-funded warrant (which equals the public offering price per share of common stock less the $0.001 per share exercise price of each such pre-funded warrant) (and excluding shares of common stock issued upon exercise of the pre-funded warrants or any resulting accounting associated therewith), after deducting underwriting discounts and commissions and estimated offering expenses payable by us and (ii) $35 million of shares of our common stock in the concurrent private placement at the purchase price of $ per share of common stock, after deducting placement agent fees and estimated offering expenses payable by us.

You should read the following table together with our consolidated financial statements and related notes to those statements and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K for the year ended December 31, 2019 and our Quarterly Report on Form 10-Q for the three months ended March 31, 2020, which are incorporated by reference into this prospectus supplement.

	As of March 31, 2020	
	Actual	As Adjusted
	(unaudited) (in thousands)	
Cash and cash equivalents	$ 108,352	$
Preferred stock, par value $0.001 per share; 5,000,000 shares authorized, no shares issued or outstanding, actual and as adjusted	—	—
Common stock, $0.001 par value: 200,000,000 shares authorized, actual and as adjusted; 41,501,639 shares issued and outstanding, actual; shares issued and outstanding, as adjusted	50	
Additional paid-in capital	600,182	
Accumulated deficit	(495,602)	
Total stockholders' equity	104,630	
Total capitalization	$ 115,714	$

The table above excludes:

- 6,635,316 shares of our common stock issuable upon the exercise of stock options outstanding as of March 31, 2020, at a weighted average exercise price of $10.69 per share;
- 1,400,701 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of March 31, 2020;
- 2,908,277 additional shares of our common stock available for future issuance under our 2013 stock incentive plan;
- 1,622,250 additional shares of our common stock available for future issuance under our 2019 inducement stock incentive plan;

- 838,182 additional shares of our common stock available for future issuance under our 2016 employee stock purchase plan; and
- 3,750,000 shares of our common stock reserved for issuance upon the exercise of pre-funded warrants outstanding as of March 31, 2020.

In addition, this table:

- assumes no exercise of the outstanding options and the outstanding pre-funded warrants described above;
- assumes no exercise by the underwriters of their option to purchase up to $ million of shares of common stock from us;
- assumes no exercise of the pre-funded warrants we are offering in this offering in lieu of common stock to certain investors; and
- does not give effect to potential future milestone payments payable in the form of shares of our common stock pursuant to (a) the agreement and plan of merger under which we acquired Inception 4, Inc., or the Inception 4 acquisition, in October 2018 or (b) the exclusive license agreement we entered into in July 2019 with the University of Massachusetts for rights to our miniCEP290 gene therapy program.

DILUTION

If you invest in our common stock or pre-funded warrants in this offering, your ownership interest will be diluted immediately to the extent of the difference between the public offering price per share of our common stock and pre-funded warrants and the as adjusted net tangible book value per share of our common stock immediately after this offering and the concurrent private placement.

Our net tangible book value as of March 31, 2020 was $104.6 million, or $2.10 per share of our common stock, based on approximately 49,731,811 shares of our common stock then outstanding. Our net tangible book value is the amount of our total tangible assets less our total liabilities. Net tangible book value per share represents our net tangible book value divided by the 49,731,811 shares of our common stock outstanding as of March 31, 2020.

After giving effect to our issuance and sale of (i) $ million of shares of our common stock and pre-funded warrants to purchase shares of our common stock in this offering at a public offering price of $ per share of common stock and $ per pre-funded warrant (which equals the price per share at which shares of common stock are being sold to the public in this offering, minus the $0.001 per share exercise price of each such pre-funded warrant) (and excluding shares of common stock issued upon exercise of the pre-funded warrants or any resulting accounting associated therewith), and after deducting underwriting discounts and commissions and estimated offering expenses payable by us and (ii) $35 million of shares of our common stock in the concurrent private placement at the purchase price of $ per share of common stock, and after deducting placement agent fees and estimated offering expenses payable by us, our as adjusted net tangible book value as of March 31, 2020 would have been $ million, or $ per share. This represents an immediate increase in as adjusted net tangible book value per share of $ to existing stockholders and immediate dilution of $ in as adjusted net tangible book value per share to new investors purchasing common stock and pre-funded warrants in this offering. Dilution per share to new investors is determined by subtracting as adjusted net tangible book value per share after this offering and the concurrent private placement from the public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis:

Public offering price per share		$
Net tangible book value per share as of March 31, 2020	$ 2.10	
Increase in net tangible book value per share attributable to new investors purchasing shares in this offering and the concurrent private placement	$	
As adjusted net tangible book value per share after this offering and the concurrent private placement		$
Dilution per share to new investors purchasing shares in this offering		$

If the underwriters exercise their option to purchase up to $ million of additional shares of our common stock in full after deducting underwriting discounts and commissions, placement agent fees and estimated offering expenses payable by us, the as adjusted net tangible book value per share of our common stock immediately after this offering and the concurrent private placement would be $ per share, representing an increase to existing stockholders of $ per share, and an immediate dilution of $ to new investors in this offering.

The table and calculations above are based on 49,731,811 shares of our common stock issued and outstanding as of March 31, 2020, and exclude the following:

- 6,635,316 shares of our common stock issuable upon the exercise of stock options outstanding as of March 31, 2020, at a weighted average exercise price of $10.69 per share;
- 1,400,701 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of March 31, 2020;
- 2,908,277 additional shares of our common stock available for future issuance under our 2013 stock incentive plan;
- 1,622,250 additional shares of our common stock available for future issuance under our 2019 inducement stock incentive plan;
- 838,182 additional shares of our common stock available for future issuance under our 2016 employee stock purchase plan; and
- 3,750,000 shares of our common stock reserved for issuance upon the exercise of pre-funded warrants outstanding as of March 31, 2020.

If any additional shares are issued in connection with the exercise of options or outstanding pre-funded warrants, or the exercise of the pre-funded warrants being offering in this offering, you will experience further dilution. In addition, to the extent we issue any additional equity securities in connection with future capital raising activities, our then-existing stockholders may experience dilution.

DESCRIPTION OF PRE-FUNDED WARRANTS

The following is a brief summary of certain terms and conditions of the pre-funded warrants being offered in this offering. The following description is subject in all respects to the provisions contained in the pre-funded warrants.

Form

The pre-funded warrants will be issued as individual warrant agreements to the purchasers. The form of pre-funded warrant will be filed as an exhibit to a Current Report on Form 8-K that we expect to file with the SEC.

Term

The pre-funded warrants will expire on the date the warrant is exercised in full.

Exercisability

The pre-funded warrants are exercisable at any time after their original issuance. The pre-funded warrants will be exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice solely by means of a cashless exercise, in which the holder would receive upon such exercise the net number of shares of our common stock determined according to the formula set forth in the pre-funded warrant. No fractional shares of our common stock will be issued in connection with the exercise of a pre-funded warrant. In lieu of fractional shares, we will pay the holder an amount in cash equal to the fractional amount multiplied by the last closing trading price of our common stock on the exercise date.

Exercise Limitations

We may not effect the exercise of any pre-funded warrant, and a holder will not be entitled to exercise any portion of any pre-funded warrant that, upon giving effect to such exercise, would cause: (i) the aggregate number of shares of our common stock beneficially owned by such holder (together with its affiliates) to exceed 9.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise; or (ii) the combined voting power of our securities beneficially owned by such holder (together with its affiliates) to exceed 9.99% of the combined voting power of all of our securities outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. However, any holder of a pre-funded warrant may increase or decrease such percentage to any other percentage not in excess of 19.99% upon at least 61 days' prior notice from the holder to us.

Exercise Price

The exercise price of our common stock purchasable upon the exercise of the pre-funded warrants is $0.001 per share. The exercise price of the pre-funded warrants and the number of shares of our common stock issuable upon exercise of the pre-funded warrants is subject to appropriate adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock, as well as upon any distribution of assets, including cash, stock or other property, to our stockholders. The exercise price of the pre-funded warrants will not be adjusted below the par value of our common stock.

Transferability

Subject to applicable laws, the pre-funded warrants may be offered for sale, sold, transferred or assigned without our consent.

Exchange Listing

There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on The Nasdaq Global Select Market, any other national securities exchange or any other nationally recognized trading system.

Fundamental Transactions

Upon the consummation of a fundamental transaction (as described in the pre-funded warrants, and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of 50% of the voting power of our outstanding common stock), the holders of the pre-funded warrants will be entitled to receive, upon exercise of the pre-funded warrants, the kind and amount of securities, cash or other property that such holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction, without regard to any limitations on exercised contained in the pre-funded warrants. Notwithstanding the foregoing, in the event of a fundamental transaction where the consideration consists solely of cash, solely of marketable securities or a combination of cash and marketable securities, then each pre-funded warrant shall automatically be deemed to be exercised in full in a cashless exercise effective immediately prior to and contingent upon the consummation of such fundamental transaction.

No Rights as a Stockholder

Except by virtue of such holder's ownership of shares of our common stock, and except for the right to participate in certain dividends and distributions, the holder of a pre-funded warrant does not have the rights or privileges of a holder of our common stock, including any voting rights, until such holder exercises the pre-funded warrant.

MATERIAL U.S. FEDERAL TAX CONSIDERATIONS FOR HOLDERS OF OUR COMMON STOCK AND PRE-FUNDED WARRANTS

The following discussion describes the material U.S. federal income tax consequences of the acquisition, ownership and disposition of our common stock and pre-funded warrants acquired in this offering. This discussion is based on the current provisions of the Internal Revenue Code of 1986, as amended, or the Code, existing and proposed U.S. Treasury regulations promulgated thereunder, and administrative rulings and court decisions in effect as of the date of this prospectus supplement, all of which are subject to change or to differing interpretation at any time, possibly with retroactive effect. Any change or differing interpretation could alter the tax consequences to holders described in this prospectus supplement. No ruling has been or will be sought from the Internal Revenue Service, or the IRS, with respect to the matters discussed below, and there can be no assurance the IRS will not take a contrary position regarding the tax consequences of the acquisition, ownership or disposition of our common stock or pre-funded warrants, or that any such contrary position would not be sustained by a court.

We assume in this discussion that the shares of our common stock and pre-funded warrants will be held as capital assets (generally, property held for investment). This discussion does not address all aspects of U.S. federal income taxes, does not discuss the potential application of the Medicare contribution tax on net investment income or the alternative minimum tax and does not address state or local taxes, U.S. federal gift and estate tax laws, except as specifically provided below with respect to non-U.S. holders, or any non-U.S. tax consequences that may be relevant to holders in light of their particular circumstances. This discussion also does not address the special tax rules applicable to particular holders, such as:

- financial institutions;
- brokers or dealers in securities;
- tax-exempt organizations;
- pension plans;
- owners that hold our common stock or pre-funded warrants as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment;
- insurance companies;
- controlled foreign corporations;
- passive foreign investment companies; and
- certain U.S. expatriates.

In addition, this discussion does not address the tax treatment of partnerships or other entities that are pass-through entities for U.S. federal income tax purposes or persons who hold their shares of our common stock or pre-funded warrants through partnerships or such other pass-through entities. A partner in a partnership or other pass-through entity that will hold our common stock or pre-funded warrants should consult his, her or its own tax advisor regarding the tax consequences of the ownership and disposition of our common stock or pre-funded warrants through a partnership or other pass-through entity, as applicable.

THIS DISCUSSION IS FOR INFORMATIONAL PURPOSES ONLY AND IS NOT, AND IS NOT INTENDED TO BE, LEGAL OR TAX ADVICE. PROSPECTIVE INVESTORS SHOULD CONSULT THEIR OWN TAX ADVISORS REGARDING THE U.S. FEDERAL, STATE, LOCAL, AND NON-U.S. INCOME, ESTATE AND OTHER TAX CONSIDERATIONS OF ACQUIRING, HOLDING AND DISPOSING OF OUR COMMON STOCK AND PRE-FUNDED WARRANTS.

For purposes of this discussion, a "U.S. holder" means a beneficial owner (other than a partnership or other pass-through entity) of our common stock or pre-funded warrants that is, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States, any state thereof, or the District of Columbia;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust if (1) a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or (2) the trust has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

A "non-U.S. holder" is, for U.S. federal income tax purposes, a beneficial owner of common stock or pre-funded warrants that is not a U.S. holder or a partnership for U.S. federal income tax purposes.

Treatment of Pre-Funded Warrants

Although it is not entirely free from doubt, a pre-funded warrant should be treated as a share of our common stock for U.S. federal income tax purposes and a holder of pre-funded warrants should generally be taxed in the same manner as a holder of common stock as described below. Accordingly, upon exercise, the holding period of a pre-funded warrant should carry over to the share of common stock received. Similarly, the tax basis of the pre-funded warrant should carry over to the share of common stock received upon exercise increased by the exercise price of $0.001. Each holder should consult his, her or its own tax advisor regarding the risks associated with the acquisition of a pre-funded warrant pursuant to this offering (including potential alternative characterizations). The balance of this discussion generally assumes that the characterization described above is respected for U.S. federal income tax purposes.

Tax Considerations Applicable to U.S. Holders

Distributions

In the event that we make distributions on our common stock or pre-funded warrants to a U.S. holder, those distributions generally will constitute dividends for U.S. federal income tax purposes to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Distributions in excess of our current and accumulated earnings and profits will constitute a return of capital that is applied against and reduces, but not below zero, a U.S. holder's adjusted tax basis in our common stock or pre-funded warrants, as applicable. Any remaining excess will be treated as gain realized on the sale or exchange of our common stock or pre-funded warrants as described below under the section titled "—Disposition of Our Common Stock or Pre-Funded Warrants."

Disposition of Our Common Stock or Pre-Funded Warrants

Upon a sale or other taxable disposition of our common stock or pre-funded warrants, a U.S. holder generally will recognize capital gain or loss in an amount equal to the difference between the amount realized and the U.S. holder's adjusted tax basis in the common stock or pre-funded warrants. Capital gain or loss will constitute long-term capital gain or loss if the U.S. holder's holding period for the common stock or pre-funded warrants exceeds one year. The deductibility of capital losses is subject to certain limitations. U.S. holders who recognize losses with respect to a

disposition of our common stock or pre-funded warrants should consult their own tax advisors regarding the tax treatment of such losses.

Information Reporting and Backup Withholding

Information reporting requirements generally will apply to payments of dividends on the common stock and pre-funded warrants and to the proceeds of a sale or other disposition of common stock and pre-funded warrants paid by us to a U.S. holder unless such U.S. holder is an exempt recipient, such as a corporation. Backup withholding will apply to those payments if the U.S. holder fails to provide the holder's taxpayer identification number, or certification of exempt status, or if the holder otherwise fails to comply with applicable requirements to establish an exemption. Backup withholding is not an additional tax. Rather, any amounts withheld under the backup withholding rules will be allowed as a refund or a credit against the U.S. holder's U.S. federal income tax liability provided the required information is timely furnished to the IRS.

Tax Considerations Applicable To Non-U.S. Holders

Distributions

In the event that we make distributions on our common stock or pre-funded warrants to a non-U.S. holder, those distributions generally will be treated in the manner described in "Tax Considerations Applicable to U.S. Holders—Distributions".

Any distribution on our common stock or pre-funded warrants that is treated as a dividend paid to a non-U.S. holder that is not effectively connected with the holder's conduct of a trade or business in the United States will generally be subject to withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and the non-U.S. holder's country of residence. To obtain a reduced rate of withholding under a treaty, a non-U.S. holder generally will be required to provide the applicable withholding agent with a properly executed IRS Form W-8BEN, IRS Form W-8BEN-E or other appropriate form, certifying the non-U.S. holder's entitlement to benefits under that treaty. Non-U.S. holders are urged to consult with their own tax advisors regarding their entitlement to benefits under a relevant income tax treaty and the specific methods available to them to satisfy these requirements.

We generally are not required to withhold tax on dividends paid to a non-U.S. holder that are effectively connected with the holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, are attributable to a permanent establishment or fixed base that the holder maintains in the United States) if a properly executed IRS Form W-8ECI, stating that the dividends are so connected, is furnished to us or, the applicable withholding agent. In general, such effectively connected dividends will be subject to U.S. federal income tax on a net income basis at the regular graduated rates applicable to U.S. persons. A corporate non-U.S. holder receiving effectively connected dividends may also be subject to an additional "branch profits tax," which is imposed, under certain circumstances, at a rate of 30% (or such lower rate as may be specified by an applicable treaty) on the corporate non-U.S. holder's effectively connected earnings and profits, subject to certain adjustments.

See also the sections below titled "—Information Reporting and Backup Withholding" and "—FATCA" for additional withholding rules that may apply to dividends paid to certain non-U.S. financial institutions or non-financial non-U.S. entities.

Disposition of Our Common Stock or Pre-Funded Warrants

Subject to the discussions below under the headings "Information Reporting and Backup Withholding" and "FATCA," a non-U.S. holder generally will not be subject to U.S. federal income or

withholding tax on any gain realized upon such non-U.S. holder's sale, exchange or other disposition of our common stock or pre-funded warrants unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a trade or business in the United States, and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States; in these cases, the non-U.S. holder generally will be taxed on a net income basis at the regular graduated rates and in the manner applicable to U.S. persons (as defined in the Code), and, if the non-U.S. holder is a non-U.S. corporation, the branch profits tax described above under the heading "Distributions" may also apply;
- the non-U.S. holder is a non-resident alien present in the United States for 183 days or more in the taxable year of the disposition and certain other requirements are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) on the net gain derived from the disposition, which may be offset by certain U.S.-source capital losses of the non-U.S. holder, if any; or
- we are or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period of the common stock or pre-funded warrants, if shorter) a "U.S. real property holding corporation" unless our common stock is regularly traded on an established securities market and the non-U.S. holder held no more than 5% of our outstanding common stock, directly or indirectly, during the shorter of the five-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Special rules may apply to the determination of the 5% threshold in the case of a holder of a pre-funded warrant. Non-U.S. holders are urged to consult their own tax advisors regarding the effect of holding our pre-funded warrants on the calculation of such 5% threshold. If we are determined to be a U.S. real property holding corporation and the foregoing exception does not apply, then the non-U.S. holder generally will be taxed on its net gain derived from the disposition at the U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Generally, a corporation is a "U.S. real property holding corporation" if the fair market value of its "U.S. real property interests" (as defined in the Code and applicable regulations) equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we believe that we are not currently, and we do not anticipate becoming, a "U.S. real property holding corporation" for U.S. federal income tax purposes. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rule described above.

See the sections titled "—Information Reporting and Backup Withholding" and "—FATCA" below for additional information regarding withholding rules that may apply to proceeds of a disposition of our common stock or pre-funded warrants paid to non-U.S. financial institutions or non-financial non-U.S. entities.

U.S. Federal Estate Tax

Shares of our common stock or pre-funded warrants that are owned or treated as owned by an individual who is a non-U.S. holder (as specially defined for U.S. federal estate tax purposes) at the time of death will be included in the individual's gross estate for U.S. federal estate tax purposes and, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

Information Reporting and Backup Withholding

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock or pre-funded warrants paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders generally will have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock or pre-funded warrants. Generally, a non-U.S. holder will comply with such procedures if it provides a properly executed IRS Form W-8BEN or W-8BEN-E (or other applicable Form W-8), or otherwise meets documentary evidence requirements for establishing that it is a non-U.S. holder, or otherwise establishes an exemption. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above under the heading "Distributions," will generally be exempt from U.S. backup withholding.

Information reporting and backup withholding generally will apply to the proceeds of a disposition of our common stock or pre-funded warrants by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or non-U.S., unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

FATCA

Provisions of the Code commonly referred to as the Foreign Account Tax Compliance Act, or FATCA, generally impose a 30% withholding tax on dividends on, and gross proceeds from the sale or other disposition of, our common stock and pre-funded warrants if paid to a non-U.S. entity unless (1) if the non-U.S. entity is a "non-U.S. financial institution," the non-U.S. entity undertakes certain due diligence, reporting, withholding, and certification obligations, (2) if the non-U.S. entity is not a "non-U.S. financial institution," the non-U.S. entity identifies certain of its U.S. investors, if any, or (3) the non-U.S. entity is otherwise excepted under FATCA.

Withholding under FATCA generally applies to payments of dividends on our common stock and pre-funded warrants. While withholding under FATCA may apply to payments of gross proceeds from a sale or other disposition of our common stock and pre-funded warrants, under proposed U.S. Treasury regulations, withholding on payments of gross proceeds is not required. Although such regulations are not final, applicable withholding agents may rely on the proposed regulations until final regulations are issued.

If withholding under FATCA is required on any payment related to our common stock or pre-funded warrants, investors not otherwise subject to withholding (or that otherwise would be entitled to a reduced rate of withholding) on such payment may be required to seek a refund or credit from the IRS. An intergovernmental agreement between the United States and an applicable non-U.S. country may modify the requirements described in this section. Non-U.S. holders should consult their own tax advisors regarding the possible implications of FATCA on their investment in our common stock or pre-funded warrants.

The preceding discussion of material U.S. federal tax considerations is for informational purposes only. It is not legal or tax advice. Prospective investors should consult their own tax advisors regarding the particular U.S. federal, state, local, and non-U.S. tax consequences of purchasing, holding and disposing of our common stock or pre-funded warrants, including the consequences of any proposed changes in applicable laws.

UNDERWRITING

We and the underwriters for the offering named below have entered into an underwriting agreement with respect to the common stock and pre-funded warrants being offered. Subject to the terms and conditions of the underwriting agreement, each underwriter has severally agreed to purchase from us the number of shares of our common stock and pre-funded warrants set forth opposite its name below. Cowen and Company, LLC and Credit Suisse Securities (USA) LLC are the representatives of the underwriters.

Underwriter	Number of Shares	Number of Pre-Funded Warrants
Cowen and Company, LLC		
Credit Suisse Securities (USA) LLC		
Wedbush Securities Inc.		
Total		

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent and that the underwriters have agreed, severally and not jointly, to purchase all of the shares and pre-funded warrants sold under the underwriting agreement if any of these shares or pre-funded warrants are purchased, other than those shares covered by the option to purchase additional shares described below. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

Our Chief Operating Officer, Keith Westby, has indicated an interest in purchasing an aggregate of approximately $80,000 of shares of our common stock in this offering at the public offering price. However, because indications of interest are not binding agreements or commitments to purchase, Mr. Westby may determine to purchase fewer shares than he indicated an interest in purchasing or not to purchase any shares in this offering. It is also possible that Mr. Westby could indicate an interest in purchasing more shares of our common stock. In addition, the underwriters could determine to sell fewer shares to Mr. Westby than Mr. Westby indicates an interest in purchasing or not to sell any shares to Mr. Westby.

We have agreed to indemnify the underwriters against specified liabilities, including liabilities under the Securities Act, and to contribute to payments the underwriters may be required to make in respect thereof.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "ISEE". There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on The Nasdaq Global Select Market, any other national securities exchange or any other nationally recognized trading system.

The underwriters are offering the shares and pre-funded warrants, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel and other conditions specified in the underwriting agreement. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Option to Purchase Additional Shares. We have granted to the underwriters an option to purchase up to $ million of additional shares of common stock at the public offering price, less the underwriting discount. This option is exercisable for a period of 30 days. To the extent that

the underwriters exercise this option, the underwriters will purchase additional shares from us in approximately the same proportion as shown in the table above.

Concurrent Private Placement. Concurrently with this offering, pursuant to the private placement agreement, we have agreed to sell to the private placement purchasers, in a private placement exempt from the registration requirements of the Securities Act and at a sale price equal to the price to the public in this offering, approximately $35 million of shares of our common stock. The consummation of the concurrent private placement is contingent on the closing of this offering and the satisfaction of certain other customary conditions. The private placement purchasers will receive certain registration rights upon the consummation of the concurrent private placement. Cowen and Company, LLC and Credit Suisse Securities (USA) LLC are serving as placement agents for the concurrent private placement for which they will receive customary placement agent fees. No underwriting discounts and commissions will be payable with respect to the concurrent private placement. The closing of the concurrent private placement is expected to occur on or about June , 2020. The consummation of this offering is not contingent on the consummation of the concurrent private placement.

Discounts and Commissions. The following table shows the public offering price, underwriting discount and proceeds, before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

We estimate that the total expenses of this offering, excluding underwriting discount, will be approximately $310,000 and are payable by us.

			Total	
	Per Share	Per Pre-Funded Warrant	Without Exercise of Option to Purchase Additional Shares	With Full Exercise of Option to Purchase Additional Shares
Public offering price				
Underwriting discount				
Proceeds, before expenses, to IVERIC bio, Inc.				

We are offering to those purchasers whose purchase of shares of common stock in this offering would result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 9.99% of our outstanding common stock following the consummation of this offering, the opportunity to purchase, in lieu of the shares of our common stock that would result in ownership in excess of 9.99%, pre-funded warrants to purchase such excess shares of our common stock. Each pre-funded warrant will have an exercise price of $0.001. The purchase price for each such pre-funded warrant would equal the per share public offering price for the common stock in this offering less the $0.001 per share exercise price of each such pre-funded warrant.

The underwriters propose to offer the shares of common stock and pre-funded warrants to the public at the public offering prices set forth on the cover of this prospectus. The underwriters may offer the shares of common stock and pre-funded warrants to securities dealers at the public offering price less a concession not in excess of $ per share of common stock and $ per pre-funded warrant. If all of the shares and pre-funded warrants are not sold at the public offering price, the underwriters may change the offering prices and other selling terms.

Discretionary Accounts. The underwriters do not intend to confirm sales of the shares or pre-funded warrants to any accounts over which they have discretionary authority.

Stabilization. In connection with this offering, the underwriters may engage in stabilizing transactions, overallotment transactions, syndicate covering transactions, penalty bids and purchases to cover positions created by short sales.

- Stabilizing transactions permit bids to purchase shares of common stock so long as the stabilizing bids do not exceed a specified maximum, and are engaged in for the purpose of preventing or retarding a decline in the market price of the common stock while the offering is in progress.
- Overallotment transactions involve sales by the underwriters of shares of common stock in excess of the number of shares the underwriters are obligated to purchase. This creates a syndicate short position which may be either a covered short position or a naked short position. In a covered short position, the number of shares overallotted by the underwriters is not greater than the number of shares that they may purchase in the overallotment option. In a naked short position, the number of shares involved is greater than the number of shares in the overallotment option. The underwriters may close out any short position by exercising their overallotment option and/or purchasing shares in the open market.
- Syndicate covering transactions involve purchases of common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared with the price at which they may purchase shares through exercise of the overallotment option. If the underwriters sell more shares than could be covered by exercise of the overallotment option and, therefore, have a naked short position, the position can be closed out only by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that after pricing there could be downward pressure on the price of the shares in the open market that could adversely affect investors who purchase in the offering.
- Penalty bids permit the representative to reclaim a selling concession from a syndicate member when the common stock originally sold by that syndicate member is purchased in stabilizing or syndicate covering transactions to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock in the open market may be higher than it would otherwise be in the absence of these transactions. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of our common stock. These transactions may be effected on the Nasdaq Stock Market, in the over-the-counter market or otherwise and, if commenced, may be discontinued at any time.

Passive Market Making. In connection with this offering, underwriters and selling group members may engage in passive market making transactions in our common stock on the Nasdaq Stock Market in accordance with Rule 103 of Regulation M under the Securities Exchange Act of 1934, as amended, during a period before the commencement of offers or sales of common stock and extending through the completion of the distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, such bid must then be lowered when specified purchase limits are exceeded.

Lock-Up Agreements. We and certain of our directors and officers have agreed that, without the prior written consent of Cowen and Company, LLC and Credit Suisse Securities (USA) LLC on behalf of the underwriters, we or such other person, will not, during the period ending 90 days after the date of this prospectus (the "restricted period"):

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of common stock beneficially owned (as such term is used in Rule 13d-3 of the Securities Exchange Act of 1934, as amended) or any securities so owned convertible into or exercisable or exchangeable for shares of common stock;
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock; or
- publicly disclose the intention to make any such offer, sale, pledge or disposition of shares of common stock;
- whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. In addition, we and each such person agrees that, without the prior written consent of Cowen and Company, LLC and Credit Suisse Securities (USA) LLC on behalf of the underwriters, we or such other person will not, during the restricted period, make any demand for, or exercise any right with respect to, the registration of any shares of common stock or any security convertible into or exercisable or exchangeable for common stock.

The restrictions described in the immediately preceding paragraph do not apply to us in respect of:

a) the sale of shares and pre-funded warrants to the underwriters in this offering and the sale of shares in the concurrent private placement; or

b) the issuance by us of shares of common stock upon the exercise of an option or warrant or the conversion of a security described in this prospectus and outstanding on the date hereof; or

c) any options and other awards granted under a stock incentive plan or stock purchase plan described in this prospectus (and the issuance of shares upon the exercise thereof); or

d) the filing by us of any registration statement on Form S-8 or a successor form thereto relating to the shares of common stock granted pursuant to or reserved for issuance under a stock incentive plan or stock purchase plan described in this prospectus or the filing by us of registration statements in accordance with the terms and conditions of the private placement agreement; or

e) the issuance by the Company of shares of common stock upon the Company's achievement of milestones under existing acquisition and licensing agreements, in each case as described in this prospectus; or

f) the issuance and sale of up to 500,000 shares of common stock at or above the then-prevailing market price in connection with a transaction that includes additional non-dilutive funding for the development of one or more of our product candidates, provided that the recipient of such shares agrees not to sell, transfer or otherwise dispose of such shares for the remainder of the restricted period without the prior written consent of Cowen

and Company, LLC and Credit Suisse Securities (USA) LLC on behalf of the underwriters; or

g) shares of common stock or other securities issued in connection with a transaction that includes a commercial relationship (including joint ventures, marketing or distribution arrangements, collaboration agreements or intellectual property license agreements) or any acquisition of assets or not less than a majority or controlling portion of the equity of another entity, provided that (x) the aggregate number of shares of common stock issued pursuant to this clause (g) shall not exceed 5.0% of the total number of outstanding shares of common stock and (y) the recipient of any such shares of common stock and securities issued pursuant to this clause (g) during the restricted period shall enter into a lock-up agreement; or

h) the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that (i) such plan does not provide for the transfer of common stock during the restricted period and (ii) to the extent a public announcement or filing under the Exchange Act, if any, is required of or voluntarily made by us regarding the establishment of such plan, such announcement or filing shall include a statement to the effect that no transfer of common stock may be made under such plan during the restricted period.

The restrictions described in the second immediately preceding paragraph do not apply to directors or officers in respect of:

a) transfers or dispositions of common stock acquired in this offering or acquired in open market transactions after the completion of this offering; or

b) the exercise of options to purchase shares of common stock granted under a stock incentive plan or stock purchase plan which is described in this prospectus or the exercise of warrants to purchase shares of common stock described in this prospectus and outstanding as of the date of this prospectus, *provided* that the underlying common stock continues to be subject to the restrictions set forth above; or

c) the exercise of options to purchase shares of common stock granted under a stock incentive plan or stock purchase plan described in this prospectus pursuant to an arrangement whereby we withhold shares issuable pursuant to such option in payment of the exercise price, *provided* that no filing under Section 16(a) of the Exchange Act or other public announcement, reporting a reduction in beneficial ownership of shares of common stock, shall be required or shall be voluntarily made during the restricted period in connection with such option exercise, and *provided* further that the underlying common stock issued upon the exercise of such options continues to be subject to the restrictions set forth above; or

d) transfers or dispositions to us of common stock or any security convertible into or exercisable or exchangeable for common stock pursuant to any contractual arrangement in effect on the date of the lock-up agreement that provides for the repurchase by us of the director's or officer's common stock or such other securities or in connection with the termination of the director's or officer's employment with us; or

e) transfers or dispositions of shares of common stock or any security convertible into or exercisable or exchangeable for common stock as a bona fide gift; or

f) transfers or dispositions of shares of common stock or any security convertible into or exercisable or exchangeable for common stock by will or other testamentary document or by intestacy; or

g) distributions of shares of common stock or any security convertible into or exercisable or exchangeable for common stock to limited partners, members, stockholders or trust beneficiaries of the directors or officers or to any investment fund or other entity controlled or managed by the directors or officers; or

h) transfers or dispositions of shares of common stock or any security convertible into or exercisable or exchangeable for common stock to any trust for the direct or indirect benefit of the director or officer or the immediate family of the director or officer in a transaction not involving a disposition for value; or

provided that (i) in the case of any transfer or distribution pursuant to clause (e), (f), (g) or (h), each donee, transferee or distributee shall sign and deliver a lock-up letter substantially in the form of the lock-up agreement and (ii) in the case of any transfer or distribution pursuant to clause (a), (e), (g) or (h), no filing under Section 16(a) of the Exchange Act or other public announcement, reporting a reduction in beneficial ownership of shares of common stock, shall be required or shall be voluntarily made during the restricted period in connection with such transfer or distribution, or

i) the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that (i) such plan does not provide for the transfer of common stock during the restricted period and (ii) to the extent a public announcement or filing under the Exchange Act, if any, is required of or voluntarily made by or on behalf of our directors or officers regarding the establishment of such plan, such announcement or filing shall include a statement to the effect that no transfer of common stock may be made under such plan during the restricted period; or

j) dispositions, or the withholding of shares of common stock, solely in connection with the payment of taxes due with respect to the vesting of restricted stock unit awards, insofar as such restricted stock units are outstanding as of the date of this prospectus, provided that to the extent a public announcement or filing under the Exchange Act, if any, is required or voluntarily made by or on behalf of us or the director or officer regarding any such disposition or withholding, such announcement or filing shall include a statement to the effect that the that the transfer relates to the payment of taxes due with respect to the vesting of such restricted stock unit awards; or k) transfers of shares pursuant to sales in the public market undertaken under a trading plan pursuant to Rule 10b5-1 under the Exchange Act, provided that such trading plan shall have been in effect prior to the date of this prospectus, and provided further that to the extent a public announcement or filing under the Exchange Act, if any, is required or voluntarily made regarding any such sales, such announcement or filing shall include a statement to the effect that sale was made pursuant to a trading plan pursuant to Rule 10b5-1 under the Exchange Act.

For purposes of the lock-up agreements "immediate family" shall mean any relationship by blood, marriage or adoption, not more remote than first cousin.

The representative, in its sole discretion, may release the common stock and other securities subject to the lock-up agreements described above in whole or in part at any time with or without notice.

Canada. The common stock and pre-funded warrants may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

European Economic Area and the United Kingdom. In relation to each Member State of the European Economic Area and the United Kingdom (each a "Relevant State"), no shares of common stock or pre-funded warrants have been offered or will be offered to the public in that Relevant State prior to the publication of a prospectus in relation to the shares of common stock or pre-funded warrants which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation, except that offers of shares of common stock and pre-funded warrants may be made to the public in that Relevant State at any time under the following exemptions under the Prospectus Regulation:

a. to any legal entity which is a qualified investor as defined under the Prospectus Regulation;

b. to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of the representatives of the underwriters for any such offer; or

c. in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of shares of common stock or pre-funded warrants shall require the Company or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

Each person in a Relevant State who initially acquires any shares of common stock or pre-funded warrants or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with the Company and the underwriters that it is a qualified investor within the meaning of the Prospectus Regulation.

In the case of any shares of common stock or pre-funded warrants being offered to a financial intermediary as that term is used in Article 5(1) of the Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares of common stock or pre-funded warrants acquired by it in the offer have not been acquired on a

non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer to the public other than their offer or resale in a Relevant State to qualified investors, as so defined or in circumstances in which the prior consent of the underwriters has been obtained to each such proposed offer or resale.

The Company, the representatives of the underwriters and their respective affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

For the purposes of this provision, the expression an "offer to the public" in relation to any shares of common stock or pre-funded warrants in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of common stock or pre-funded warrants to be offered so as to enable an investor to decide to purchase or subscribe for any shares of common stock, and the expression "Prospectus Regulation" means Regulation (EU) 2017/1129.

References to the Prospectus Regulation includes, in relation to the UK, the Prospectus Regulation as it forms part of UK domestic law by virtue of the European Union (Withdrawal) Act 2018.

The above selling restriction is in addition to the other selling restrictions set out herein.

Switzerland. The securities will not be offered, directly or indirectly, to the public in Switzerland and this prospectus does not constitute a public offering prospectus as that term is understood pursuant to article 652a or 1156 of the Swiss Federal Code of Obligations.

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

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728-1968. In particular, we may request, as a condition to be offered common stock or pre-funded warrants, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728-1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728-1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728-1968 and the regulations promulgated thereunder in connection with the offer to be issued common stock; (iv) that the shares of common stock and pre-funded warrants that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728-1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of

the Israeli Securities Law, 5728-1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor's name, address and passport number or Israeli identification number.

United Kingdom. In the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who (i) have professional experience in matters relating to investments and who qualify as investment professionals within the meaning of Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (as amended, the "Financial Promotion Order"), (ii) are persons falling within Article 49(2)(a) to (d) ("high net worth companies, unincorporated associations etc.") of the Financial Promotion Order, (iii) are outside the United Kingdom, or (iv) are persons to whom an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000, as amended ("FSMA")) in connection with the issue or sale of any securities may otherwise lawfully be communicated or caused to be communicated (all such persons together being referred to as "relevant persons"). This document is directed only at relevant persons and must not be acted on or relied on by persons who are not relevant persons. Any investment or investment activity to which this document relates is available only to relevant persons and will be engaged in only with relevant persons.

We have not authorized and do not authorize the making of any offer of securities through any financial intermediary on our behalf, other than offers made by the underwriters and their respective affiliates, with a view to the final placement of the securities as contemplated in this document. Accordingly, no purchaser of the shares or pre-funded warrants, other than the underwriters, is authorized to make any further offer of shares or pre-funded warrants on our behalf or on behalf of the underwriters.

Electronic Offer, Sale and Distribution of Shares. A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters or selling group members, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute prospectuses electronically. The representative may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters and selling group members that will make internet distributions on the same basis as other allocations. Other than the prospectus in electronic format, the information on these websites is not part of this prospectus or the registration statement of which this prospectus forms a part, has not been approved or endorsed by us or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

Other Relationships. In addition, Cowen and Company, LLC and Credit Suisse Securities (USA) LLC are serving as placement agents for the concurrent private placement and will be receiving customary placement agent fees in connection therewith. Certain of the underwriters and their affiliates have provided, and may in the future provide, various investment banking, commercial banking and other financial services for us and our affiliates for which they have received, and may in the future receive, customary fees. Cowen and Company, LLC was the sales agent under our sales agreement for our "at-the-market" equity offering program. As of the date of this prospectus supplement, such sales agreement has been terminated and the "at-the-market" equity offering program pursuant to the sales agreement is no longer available to us.

LEGAL MATTERS

The validity of the securities offered hereby is being passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP. Davis Polk & Wardwell LLP is acting as counsel for the underwriters in connection with this offering.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements, included in our Annual Report on Form 10-K for the year ended December 31, 2019, and the effectiveness of our internal control over financial reporting as of December 31, 2019, as set forth in their reports, which are incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our consolidated financial statements and our management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2019 are incorporated herein by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at http://www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at www.ivericbio.com. Our website is not a part of this prospectus supplement and is not incorporated by reference in this prospectus supplement.

This prospectus supplement is part of a registration statement we filed with the SEC. This prospectus supplement omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the accompanying prospectus and the registration statement for further information about us and our consolidated subsidiaries and the securities we are offering. Statements in this prospectus supplement concerning any document we filed as an exhibit to the accompany prospectus, the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements. You can obtain a copy of the accompanying prospectus and the registration statement from the SEC's website.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference in this prospectus supplement much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus supplement and the accompanying prospectus is considered to be part of this prospectus supplement. Because we are incorporating by reference future filings with the SEC, this prospectus supplement is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus supplement. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement or the accompanying prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus supplement incorporates by reference the documents listed below (File No. 001-36080) and any

future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) until the offering of the securities under the registration statement is terminated or completed:

- Annual Report on Form 10-K for the fiscal year ended December 31, 2019, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our definitive proxy statement for the 2020 Annual Meeting of Stockholders, filed April 28, 2020;
- Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2020;
- Current Reports on Form 8-K filed on January 13, 2020 (excluding Item 2.02), March 18, 2020, June 10, 2020, June 15, 2020 and June 17, 2020; and
- The description of our common stock contained in our Registration Statement on Form 8-A filed on September 20, 2013, including any amendments or reports filed for the purpose of updating such description.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

IVERIC bio, Inc.
One Penn Plaza, 35th Floor
New York, NY 10119
(212) 845-8200

$150,000,000

PROSPECTUS

Ophthotech Corporation

Debt Securities
Common Stock
Preferred Stock
Depositary Shares
Units
Warrants

We may offer and sell securities from time to time in one or more offerings of up to $150,000,000 in aggregate offering price. This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide the specific terms of these securities in supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. You should read this prospectus and any applicable prospectus supplement before you invest.

We may offer these securities in amounts, at prices and on terms determined at the time of offering. The securities may be sold directly to you, through agents, or through underwriters and dealers. If agents, underwriters or dealers are used to sell the securities, we will name them and describe their compensation in a prospectus supplement.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "OPHT."

Investing in these securities involves significant risks. See "Risk Factors" included in any accompanying prospectus supplement and in the documents incorporated by reference in this prospectus for a discussion of the factors you should carefully consider before deciding to purchase these securities.

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

The date of this prospectus is August 15, 2018

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, which we refer to as the SEC, utilizing a "shelf" registration process. Under this shelf registration process, we may from time to time sell any combination of the securities described in this prospectus in one or more offerings for an aggregate initial offering price of up to $150,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the accompanying prospectus supplement together with the additional information described under the heading "Where You Can Find More Information" beginning on page 3 of this prospectus.

You should rely only on the information contained in or incorporated by reference in this prospectus, any accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not authorized anyone to provide you with different information. This prospectus and any accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in this prospectus or such accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context otherwise indicates, references in this prospectus to "Ophthotech," "we," "our," "us" and "the Company" refer, collectively, to Ophthotech Corporation, a Delaware corporation, and its consolidated subsidiaries.

RISK FACTORS

Investing in our securities involves significant risks. You should carefully consider the risks and uncertainties described in this prospectus and any accompanying prospectus supplement, including the risk factors set forth in our filings with the SEC that are incorporated by reference herein, before making an investment decision pursuant to this prospectus and any accompanying prospectus supplement relating to a specific offering.

Our business, financial condition and results of operations could be materially and adversely affected by any or all of these risks or by additional risks and uncertainties not presently known to us or that we currently deem immaterial that may adversely affect us in the future.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at http://www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at http://www.ophthotech.com. Our website is not a part of this prospectus and is not incorporated by reference in this prospectus. You may also read and copy any document we file at the SEC's Public Reference Room, 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

This prospectus is part of a registration statement we filed with the SEC. This prospectus omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information about us and the securities we are offering. Statements in this prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's website.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus incorporates by reference the documents listed below (File No. 001-36080) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) between the date of the initial registration statement and the effectiveness of the registration statement and following the effectiveness of the registration statement until the offering of the securities under the registration statement is terminated or completed:

- Annual Report on Form 10-K for the fiscal year ended December 31, 2017, filed on March 5, 2018, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our definitive proxy statement for the 2018 Annual Meeting of Stockholders;
- Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2018, filed on May 9, 2018, and June 30, 2018, filed on August 1, 2018;
- Current Reports on Form 8-K filed on January 5, 2018, January 19, 2018, May 14, 2018, May 29, 2018, June 7, 2018 and July 5, 2018; and
- The description of our common stock contained in our Registration Statement on Form 8-A filed on September 20, 2013, including any amendments or reports filed for the purpose of updating such description.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

Ophthotech Corporation
One Penn Plaza, 35th Floor
New York, NY 10119
(212) 845-8200

FORWARD-LOOKING STATEMENTS

This prospectus and the information incorporated by reference in this prospectus include "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Exchange Act. All statements, other than statements of historical facts, contained or incorporated by reference in this prospectus, 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. In addition, any statements that refer to the potential benefits of our business plan and strategy to develop Zimura® (avacincaptad pegol) in age-related retinal diseases or autosomal recessive Stargardt disease and our gene therapy product candidate for rhodopsin-mediated autosomal dominant retinitis pigmentosa and to potentially expand our product pipeline, including through collaborative gene therapy research programs; our ability to in-license or acquire additional products, product candidates or technologies to treat ophthalmic diseases and the timing, costs, conduct and outcome of preclinical development or clinical trials we undertake for these newly acquired assets; 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 clinical trials, including statements regarding the timing of the initiation of and completion of enrollment in such trials, and the costs to obtain and timing of receipt of initial results from, and the completion of, such trials; 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; the potential advantages of our product candidates; the rate and degree of potential market acceptance and clinical utility of our product candidates, if approved; our estimates regarding the potential market opportunity for our product candidates; the potential receipt of revenue from potential future collaborations; the potential receipt of revenues from future sales of our product candidates, if approved; our sales, marketing and distribution capabilities and strategy; our ability to establish and maintain arrangements for the manufacture of our product candidates; our intellectual property position; the impact of existing and new governmental laws and regulations; and our competitive position are forward-looking statements.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you 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. See the "Risk Factors" section of this prospectus for more information. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. 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 law.

OPHTHOTECH CORPORATION

We are a science-driven biopharmaceutical company specializing in the development of novel therapies to treat ophthalmic diseases, with a focus on age-related and orphan retinal diseases. Our multi-track strategy is to leverage our clinical experience and retina expertise to develop therapies for large market, age-related retinal diseases, where unmet medical needs remain for these patients, and for orphan eye diseases with a focus on underserved patients, and to utilize a disciplined business development approach to obtain additional products, product candidates and technologies in these disease areas. We believe that there are advantages to pursuing drug development for orphan indications, including the potential for regulatory exclusivity, the potential for clinical trials with smaller sample sizes and the potential for accelerated development timelines. Our team has significant ophthalmic drug development experience and deep relationships with global ophthalmology thought leaders. We have an extensive network of ophthalmic clinical trial sites, having worked with over 250 sites worldwide. We believe that the combination of these factors, together with our experience in designing and executing IND-enabling studies and clinical trials for eye diseases, and specifically back of the eye diseases, provide us a competitive advantage.

Our principal executive offices are located at One Penn Plaza, 35th Floor, New York, NY 10119, and our telephone number is (212) 845-8200.

RATIO OF EARNINGS TO FIXED CHARGES

The following table sets forth our ratio of earnings to fixed charges for each of the periods indicated. You should read this table in conjunction with the financial statements and notes incorporated by reference in this prospectus.

	Six Months Ended	Fiscal Year Ended				
	June 30, 2018	December 31, 2017	December 31, 2016	December 31, 2015	December 31, 2014	December 31, 2013
Ratio of earnings to fixed charges	N/A	91.7	N/A	N/A	N/A	N/A

For purposes of calculating the ratios above, earnings consist of net income (loss) from continuing operations before taxes, plus fixed charges. Fixed charges include interest expense and the interest portion of rent expense which is deemed to be representative of the interest factor.

We did not record earnings for the six months ended June 30, 2018 or for the years ended December 31, 2016, 2015, 2014 and 2013. Accordingly, our earnings were insufficient to cover fixed charges for such periods and we are unable to disclose a ratio of earnings to fixed charges for such periods. The dollar amount of the deficiency in earnings available for fixed charges for the six months ended June 30, 2018 and for the years ended December 31, 2016, 2015, 2014 and 2013 was $27.1 million, $193.8 million, $122.5 million, $80.3 million, and $51.1 million, respectively.

Our ratios of earnings to combined fixed charges and preferred stock dividends for each of the periods indicated above are the same as our ratios of earnings to fixed charges set forth above.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus for general corporate purposes unless otherwise indicated in the applicable prospectus supplement. General corporate purposes may include research and development costs, the acquisition or in-license of other products, product candidates, businesses or technologies, repayment and refinancing of debt, working capital and capital expenditures. We may temporarily invest the net proceeds in a variety of capital preservation instruments, including short-term, investment grade, interest bearing instruments and U.S. government securities, until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

DESCRIPTION OF DEBT SECURITIES

We may offer debt securities, which may be senior or subordinated. We refer to the senior debt securities and the subordinated debt securities collectively as debt securities. The following description summarizes the general terms and provisions of the debt securities. We will describe the specific terms of the debt securities and the extent, if any, to which the general provisions summarized below apply to any series of debt securities in the prospectus supplement relating to the series and any applicable free writing prospectus that we authorize to be delivered. When we refer to "the Company," "we," "our," and "us" in this section, we mean Ophthotech Corporation excluding, unless the context otherwise requires or as otherwise expressly stated, our subsidiaries.

We may issue senior debt securities from time to time, in one or more series under a senior indenture to be entered into between us and a senior trustee to be named in a prospectus supplement, which we refer to as the senior trustee. We may issue subordinated debt securities from time to time, in one or more series under a subordinated indenture to be entered into between us and a subordinated trustee to be named in a prospectus supplement, which we refer to as the subordinated trustee. The forms of senior indenture and subordinated indenture are filed as exhibits to the registration statement of which this prospectus forms a part. The senior indenture and the subordinated indenture are referred to individually as an indenture and together as the indentures, and the senior trustee and the subordinated trustee are referred to individually as a trustee and together as the trustees. This section summarizes some of the provisions of the indentures and is qualified in its entirety by the specific text of the indentures, including definitions of terms used in the indentures. Wherever we refer to particular sections of, or defined terms in, the indentures, those sections or defined terms are incorporated by reference in this prospectus or the applicable prospectus supplement. You should review the indentures that are filed as exhibits to the registration statement of which this prospectus forms a part for additional information.

Neither indenture will limit the amount of debt securities that we may issue. The applicable indenture will provide that debt securities may be issued up to an aggregate principal amount authorized from time to time by us and may be payable in any currency or currency unit designated by us or in amounts determined by reference to an index.

General

The senior debt securities will constitute our unsecured and unsubordinated general obligations and will rank equally in right of payment with our other unsecured and unsubordinated obligations. The subordinated debt securities will constitute our unsecured and subordinated general obligations and will be junior in right of payment to our senior indebtedness (including senior debt securities), as described under the heading "—Certain Terms of the Subordinated Debt Securities—Subordination." The debt securities will be structurally subordinated to all existing and future indebtedness and other liabilities of our subsidiaries unless such subsidiaries expressly guarantee such debt securities.

The debt securities will be our unsecured obligations. Any secured debt or other secured obligations will be effectively senior to the debt securities to the extent of the value of the assets securing such debt or other obligations.

The applicable prospectus supplement and any free writing prospectus will include any additional or different terms of the debt securities of any series being offered, including the following terms:

- the title and type of the debt securities;
- whether the debt securities will be senior or subordinated debt securities, and, with respect to any subordinated debt securities the terms on which they are subordinated;
- the initial aggregate principal amount of the debt securities;

- the price or prices at which we will sell the debt securities;
- the maturity date or dates of the debt securities and the right, if any, to extend such date or dates;
- the rate or rates, if any, at which the debt securities will bear interest, or the method of determining such rate or rates;
- the date or dates from which such interest will accrue, the interest payment dates on which such interest will be payable or the method of determination of such dates;
- the right, if any, to extend the interest payment periods and the duration of that extension;
- the manner of paying principal and interest and the place or places where principal and interest will be payable;
- provisions for a sinking fund, purchase fund or other analogous fund, if any;
- any redemption dates, prices, obligations and restrictions on the debt securities;
- the currency, currencies or currency units in which the debt securities will be denominated and the currency, currencies or currency units in which principal and interest, if any, on the debt securities may be payable;
- any conversion or exchange features of the debt securities;
- whether the debt securities will be subject to the defeasance provisions in the indenture;
- whether the debt securities will be issued in definitive or global form or in definitive form only upon satisfaction of certain conditions;
- whether the debt securities will be guaranteed as to payment or performance;
- any special tax implications of the debt securities;
- any events of default or covenants in addition to or in lieu of those set forth in the indenture; and
- any other material terms of the debt securities.

When we refer to "principal" in this section with reference to the debt securities, we are also referring to "premium, if any."

We may from time to time, without notice to or the consent of the holders of any series of debt securities, create and issue further debt securities of any such series ranking equally with the debt securities of such series in all respects (or in all respects other than (1) the payment of interest accruing prior to the issue date of such further debt securities or (2) the first payment of interest following the issue date of such further debt securities). Such further debt securities may be consolidated and form a single series with the debt securities of such series and have the same terms as to status, redemption or otherwise as the debt securities of such series.

You may present debt securities for exchange and you may present debt securities for transfer in the manner, at the places and subject to the restrictions set forth in the debt securities and the applicable prospectus supplement. We will provide you those services without charge, although you may have to pay any tax or other governmental charge payable in connection with any exchange or transfer, as set forth in the indenture.

Debt securities may bear interest at a fixed rate or a floating rate. Debt securities bearing no interest or interest at a rate that at the time of issuance is below the prevailing market rate (original issue discount securities) may be sold at a discount below their stated principal amount. U.S. federal

income tax considerations applicable to any such discounted debt securities or to certain debt securities issued at par which are treated as having been issued at a discount for U.S. federal income tax purposes will be described in the applicable prospectus supplement.

We may issue debt securities with the principal amount payable on any principal payment date, or the amount of interest payable on any interest payment date, to be determined by reference to one or more currency exchange rates, securities or baskets of securities, commodity prices or indices. You may receive a payment of principal on any principal payment date, or a payment of interest on any interest payment date, that is greater than or less than the amount of principal or interest otherwise payable on such dates, depending on the value on such dates of the applicable currency, security or basket of securities, commodity or index. Information as to the methods for determining the amount of principal or interest payable on any date, the currencies, securities or baskets of securities, commodities or indices to which the amount payable on such date is linked and certain related tax considerations will be set forth in the applicable prospectus supplement.

Certain Terms of the Senior Debt Securities

Covenants. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the senior debt securities will not contain any financial or restrictive covenants, including covenants restricting either us or any of our subsidiaries from incurring, issuing, assuming or guaranteeing any indebtedness secured by a lien on any of our or our subsidiaries' property or capital stock, or restricting either us or any of our subsidiaries from entering into sale and leaseback transactions.

Consolidation, Merger and Sale of Assets. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, we may not consolidate with or merge into any other person, in a transaction in which we are not the surviving corporation, or convey, transfer or lease our properties and assets substantially as an entirety to any person, in either case, unless:

- the successor entity, if any, is a U.S. corporation, limited liability company, partnership or trust;
- the successor entity assumes our obligations on the senior debt securities and under the senior indenture;
- immediately after giving effect to the transaction, no default or event of default shall have occurred and be continuing; and
- we have delivered to the senior trustee an officer's certificate and an opinion of counsel, each stating that the consolidation, merger, conveyance, transfer or lease and, if a supplemental indenture is required in connection with such transaction, such supplemental indenture, comply with the senior indenture and all conditions precedent provided for in the senior indenture relating to such transaction have been complied with.

The restrictions described in the bullets above do not apply (1) to our consolidation with or merging into one of our affiliates, if our board of directors determines in good faith that the purpose of the consolidation or merger is principally to change our state of incorporation or our form of organization to another form or (2) if we merge with or into a single direct or indirect wholly-owned subsidiary of ours.

The surviving business entity will succeed to, and be substituted for, us under the senior indenture and the senior debt securities and, except in the case of a lease, we shall be released from all obligations under the senior indenture and the senior debt securities.

No Protection in the Event of a Change in Control. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the senior debt securities will not contain any provisions that may afford holders of the senior debt securities protection in the event

we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control).

Events of Default. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the following are events of default under the senior indenture with respect to senior debt securities of each series:

- failure to pay interest on any senior debt securities of such series when due and payable, if that default continues for a period of 30 days (or such other period as may be specified for such series);
- failure to pay principal on the senior debt securities of such series when due and payable whether at maturity, upon redemption, by declaration or otherwise (and, if specified for such series, the continuance of such failure for a specified period);
- default in the performance of or breach of any of our covenants or agreements in the senior indenture applicable to senior debt securities of such series, other than a covenant breach which is specifically dealt with elsewhere in the senior indenture, and that default or breach continues for a period of 90 days after we receive written notice from the trustee or from the holders of 25% or more in aggregate principal amount of the senior debt securities of such series;
- certain events of bankruptcy or insolvency, whether or not voluntary; and
- any other event of default provided for in such series of senior debt securities as may be specified in the applicable prospectus supplement.

The default by us under any other debt, including any other series of debt securities, is not a default under the senior indenture.

If an event of default other than an event of default specified in the fourth bullet point above occurs with respect to a series of senior debt securities and is continuing under the senior indenture, then, and in each such case, either the trustee or the holders of not less than 25% in aggregate principal amount of such series then outstanding under the senior indenture (each such series voting as a separate class) by written notice to us and to the trustee, if such notice is given by the holders, may, and the trustee at the request of such holders shall, declare the principal amount of and accrued interest on such series of senior debt securities to be immediately due and payable, and upon this declaration, the same shall become immediately due and payable.

If an event of default specified in the fourth bullet point above occurs and is continuing, the entire principal amount of and accrued interest on each series of senior debt securities then outstanding shall automatically become immediately due and payable.

Unless otherwise specified in the prospectus supplement relating to a series of senior debt securities originally issued at a discount, the amount due upon acceleration shall include only the original issue price of the senior debt securities, the amount of original issue discount accrued to the date of acceleration and accrued interest, if any.

Upon certain conditions, declarations of acceleration may be rescinded and annulled and past defaults may be waived by the holders of a majority in aggregate principal amount of all the senior debt securities of such series affected by the default, each series voting as a separate class. Furthermore, subject to various provisions in the senior indenture, the holders of a majority in aggregate principal amount of a series of senior debt securities, by notice to the trustee, may waive a continuing default or event of default with respect to such senior debt securities and its consequences, except a default in the payment of principal of or interest on such senior debt securities (other than any such default in payment resulting solely from an acceleration of the senior debt securities) or in respect of a covenant or provision of the senior indenture which cannot be modified or amended

without the consent of the holders of each such senior debt security. Upon any such waiver, such default shall cease to exist, and any event of default with respect to such senior debt securities shall be deemed to have been cured, for every purpose of the senior indenture; but no such waiver shall extend to any subsequent or other default or event of default or impair any right consequent thereto.

The holders of a majority in aggregate principal amount of a series of senior debt securities may direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to such senior debt securities. However, the trustee may refuse to follow any direction that conflicts with law or the senior indenture, that may involve the trustee in personal liability or that the trustee determines in good faith may be unduly prejudicial to the rights of holders of such series of senior debt securities not joining in the giving of such direction and may take any other action it deems proper that is not inconsistent with any such direction received from holders of such series of senior debt securities. A holder may not pursue any remedy with respect to the senior indenture or any series of senior debt securities unless:

- the holder gives the trustee written notice of a continuing event of default;
- the holders of at least 25% in aggregate principal amount of such series of senior debt securities make a written request to the trustee to pursue the remedy in respect of such event of default;
- the requesting holder or holders offer the trustee indemnity satisfactory to the trustee against any costs, liability or expense;
- the trustee does not comply with the request within 60 days after receipt of the request and the offer of indemnity; and
- during such 60-day period, the holders of a majority in aggregate principal amount of such series of senior debt securities do not give the trustee a direction that is inconsistent with the request.

These limitations, however, do not apply to the right of any holder of a senior debt security of any affected series to receive payment of the principal of and interest on such senior debt security in accordance with the terms of such debt security, or to bring suit for the enforcement of any such payment in accordance with the terms of such debt security, on or after the due date for the senior debt securities, which right shall not be impaired or affected without the consent of the holder.

The senior indenture requires certain of our officers to certify, on or before a fixed date in each year in which any senior debt security is outstanding, as to their knowledge of our compliance with all covenants, agreements and conditions under the senior indenture.

Satisfaction and Discharge. We can satisfy and discharge our obligations to holders of any series of debt securities if:

- we have paid or caused to be paid the principal of and interest on all senior debt securities of such series (with certain limited exceptions) when due and payable; or
- we deliver to the senior trustee for cancellation all senior debt securities of such series theretofore authenticated under the senior indenture (with certain limited exceptions); or
- all senior debt securities of such series have become due and payable or will become due and payable within one year (or are to be called for redemption within one year under arrangements satisfactory to the senior trustee) and we deposit in trust an amount of cash or a combination of cash and U.S. government or U.S. government agency obligations (or in the case of senior debt securities denominated in a foreign currency, foreign government securities or foreign government agency securities) sufficient to make interest, principal and any other payments on the debt securities of that series on their various due dates;

and if, in any such case, we also pay or cause to be paid all other sums payable under the senior indenture, as and when the same shall be due and payable and we deliver to the senior trustee an officer's certificate and an opinion of counsel, each stating that these conditions have been satisfied.

Under current U.S. federal income tax law, the deposit and our legal release from the debt securities would be treated as though we took back your debt securities and gave you your share of the cash and debt securities or bonds deposited in trust. In that event, you could recognize gain or loss on the debt securities you give back to us. Purchasers of the debt securities should consult their own advisers with respect to the tax consequences to them of such deposit and discharge, including the applicability and effect of tax laws other than the U.S. federal income tax law.

Defeasance. Unless the applicable prospectus supplement provides otherwise, the following discussion of legal defeasance and covenant defeasance will apply to any series of debt securities issued under the indentures.

Legal Defeasance. We can legally release ourselves from any payment or other obligations on the debt securities of any series (called "legal defeasance") if certain conditions are met, including the following:

- We deposit in trust for your benefit and the benefit of all other direct holders of the debt securities of the same series cash or a combination of cash and U.S. government or U.S. government agency obligations (or, in the case of senior debt securities denominated in a foreign currency, foreign government or foreign government agency obligations) that will generate enough cash to make interest, principal and any other payments on the debt securities of that series on their various due dates.

- There is a change in current U.S. federal income tax law or an IRS ruling that lets us make the above deposit without causing you to be taxed on the debt securities any differently than if we did not make the deposit and instead repaid the debt securities ourselves when due. Under current U.S. federal income tax law, the deposit and our legal release from the debt securities would be treated as though we took back your debt securities and gave you your share of the cash and debt securities or bonds deposited in trust. In that event, you could recognize gain or loss on the debt securities you give back to us.

- We deliver to the trustee a legal opinion of our counsel confirming the tax law change or ruling described above.

If we accomplish legal defeasance, as described above, you would have to rely solely on the trust deposit for repayment of the debt securities. You could not look to us for repayment in the event of any shortfall.

Covenant Defeasance. Without any change in current U.S. federal tax law, we can make the same type of deposit described above and be released from some of the covenants in the debt securities (called "covenant defeasance"). In that event, you would lose the protection of those covenants but would gain the protection of having money and securities set aside in trust to repay the debt securities. In order to achieve covenant defeasance, we must do the following (among other things):

- We must deposit in trust for your benefit and the benefit of all other direct holders of the debt securities of the same series cash or a combination of cash and U.S. government or U.S. government agency obligations (or, in the case of senior debt securities denominated in a foreign currency, foreign government or foreign government agency obligations) that will generate enough cash to make interest, principal and any other payments on the debt securities of that series on their various due dates.

- We must deliver to the trustee a legal opinion of our counsel confirming that under current U.S. federal income tax law we may make the above deposit without causing you to be taxed on the debt securities any differently than if we did not make the deposit and instead repaid the debt securities ourselves when due.

If we accomplish covenant defeasance, you could still look to us for repayment of the debt securities if there were a shortfall in the trust deposit. In fact, if one of the events of default occurred (such as our bankruptcy) and the debt securities become immediately due and payable, there may be such a shortfall. Depending on the events causing the default, you may not be able to obtain payment of the shortfall.

Modification and Waiver. We and the trustee may amend or supplement the senior indenture or the senior debt securities of any series without the consent of any holder:

- to convey, transfer, assign, mortgage or pledge any assets as security for the senior debt securities of one or more series;
- to evidence the succession of a corporation, limited liability company, partnership or trust to us, and the assumption by such successor of our covenants, agreements and obligations under the senior indenture or to otherwise comply with the covenant relating to mergers, consolidations and sales of assets;
- to comply with requirements of the SEC in order to effect or maintain the qualification of the senior indenture under the Trust Indenture Act of 1939, as amended (the "Trust Indenture Act");
- to add to our covenants such new covenants, restrictions, conditions or provisions for the protection of the holders, and to make the occurrence, or the occurrence and continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default;
- to cure any ambiguity, defect or inconsistency in the senior indenture or in any supplemental indenture or to conform the senior indenture or the senior debt securities to the description of senior debt securities of such series set forth in this prospectus or any applicable prospectus supplement;
- to provide for or add guarantors with respect to the senior debt securities of any series;
- to establish the form or forms or terms of the senior debt securities as permitted by the senior indenture;
- to evidence and provide for the acceptance of appointment under the senior indenture by a successor trustee, or to make such changes as shall be necessary to provide for or facilitate the administration of the trusts in the senior indenture by more than one trustee;
- to add to, change or eliminate any of the provisions of the senior indenture in respect of one or more series of senior debt securities, provided that any such addition, change or elimination shall (a) neither (1) apply to any senior debt security of any series created prior to the execution of such supplemental indenture and entitled to the benefit of such provision nor (2) modify the rights of the holder of any such senior debt security with respect to such provision or (b) become effective only when there is no senior debt security described in clause (a)(1) outstanding;
- to make any change to the senior debt securities of any series so long as no senior debt securities of such series are outstanding; or

- to make any change that does not adversely affect the rights of any holder in any material respect.

Other amendments and modifications of the senior indenture or the senior debt securities issued may be made, and our compliance with any provision of the senior indenture with respect to any series of senior debt securities may be waived, with the consent of the holders of a majority of the aggregate principal amount of the outstanding senior debt securities of each series affected by the amendment or modification (voting as separate series); provided, however, that each affected holder must consent to any modification, amendment or waiver that:

- extends the final maturity of any senior debt securities of such series;
- reduces the principal amount of any senior debt securities of such series;
- reduces the rate, or extends the time for payment of, interest on any senior debt securities of such series;
- reduces the amount payable upon the redemption of any senior debt securities of such series;
- changes the currency of payment of principal of or interest on any senior debt securities of such series;
- reduces the principal amount of original issue discount securities payable upon acceleration of maturity or the amount provable in bankruptcy;
- waives a continuing default in the payment of principal of or interest on the senior debt securities (other than any such default in payment resulting solely from an acceleration of the senior debt securities);
- changes the provisions relating to the waiver of past defaults or impairs the right of holders to receive payment or to institute suit for the enforcement of any payment or conversion of any senior debt securities of such series on or after the due date therefor;
- modifies any of the provisions of these restrictions on amendments and modifications, except to increase any required percentage or to provide that certain other provisions cannot be modified or waived without the consent of the holder of each senior debt security of such series affected by the modification;
- adversely affects the right to convert or exchange senior debt securities into common stock or other property in accordance with the terms of the senior debt securities; or
- reduces the above-stated percentage of outstanding senior debt securities of such series whose holders must consent to a supplemental indenture or modifies or amends or waives certain provisions of or defaults under the senior indenture.

It shall not be necessary for the holders to approve the particular form of any proposed amendment, supplement or waiver, but it shall be sufficient if the holders' consent approves the substance thereof. After an amendment, supplement or waiver of the senior indenture in accordance with the provisions described in this section becomes effective, the trustee must give to the holders affected thereby certain notice briefly describing the amendment, supplement or waiver. Any failure by the trustee to give such notice, or any defect therein, shall not, however, in any way impair or affect the validity of any such amendment, supplemental indenture or waiver.

No Personal Liability of Incorporators, Stockholders, Officers, Directors. The senior indenture provides that no recourse shall be had under any obligation, covenant or agreement of ours in the senior indenture or any supplemental indenture, or in any of the senior debt securities or because of the creation of any indebtedness represented thereby, against any of our incorporators, stockholders, officers or directors, past, present or future, or of any predecessor or successor entity thereof under any

law, statute or constitutional provision or by the enforcement of any assessment or by any legal or equitable proceeding or otherwise. Each holder, by accepting the senior debt securities, waives and releases all such liability.

Concerning the Trustee. The senior indenture provides that, except during the continuance of an event of default, the trustee will not be liable except for the performance of such duties as are specifically set forth in the senior indenture. If an event of default has occurred and is continuing, the trustee will exercise such rights and powers vested in it under the senior indenture and will use the same degree of care and skill in its exercise as a prudent person would exercise under the circumstances in the conduct of such person's own affairs.

The senior indenture and the provisions of the Trust Indenture Act incorporated by reference therein contain limitations on the rights of the trustee thereunder, should it become a creditor of ours or any of our subsidiaries, to obtain payment of claims in certain cases or to realize on certain property received by it in respect of any such claims, as security or otherwise. The trustee is permitted to engage in other transactions, provided that if it acquires any conflicting interest (as defined in the Trust Indenture Act), it must eliminate such conflict or resign.

We may have normal banking relationships with the senior trustee in the ordinary course of business.

Unclaimed Funds. All funds deposited with the trustee or any paying agent for the payment of principal, premium, interest or additional amounts in respect of the senior debt securities that remain unclaimed for two years after the date upon which such amounts became due and payable will be repaid to us. Thereafter, any right of any holder of senior debt securities to such funds shall be enforceable only against us, and the trustee and paying agents will have no liability therefor.

Governing Law. The senior indenture and the senior debt securities will be governed by, and construed in accordance with, the internal laws of the State of New York.

Certain Terms of the Subordinated Debt Securities

Other than the terms of the subordinated indenture and subordinated debt securities relating to subordination or otherwise as described in the prospectus supplement relating to a particular series of subordinated debt securities, the terms of the subordinated indenture and subordinated debt securities are identical in all material respects to the terms of the senior indenture and senior debt securities.

Additional or different subordination terms may be specified in the prospectus supplement applicable to a particular series.

Subordination. The indebtedness evidenced by the subordinated debt securities is subordinate to the prior payment in full of all of our senior indebtedness, as defined in the subordinated indenture. During the continuance beyond any applicable grace period of any default in the payment of principal, premium, interest or any other payment due on any of our senior indebtedness, we may not make any payment of principal of or interest on the subordinated debt securities (except for certain sinking fund payments). In addition, upon any payment or distribution of our assets upon any dissolution, winding-up, liquidation or reorganization, the payment of the principal of and interest on the subordinated debt securities will be subordinated to the extent provided in the subordinated indenture in right of payment to the prior payment in full of all our senior indebtedness. Because of this subordination, if we dissolve or otherwise liquidate, holders of our subordinated debt securities may receive less, ratably, than holders of our senior indebtedness. The subordination provisions do not prevent the occurrence of an event of default under the subordinated indenture.

The term "senior indebtedness" of a person means with respect to such person the principal of, premium, if any, interest on, and any other payment due pursuant to any of the following, whether outstanding on the date of the subordinated indenture or incurred by that person in the future:

- all of the indebtedness of that person for money borrowed;
- all of the indebtedness of that person evidenced by notes, debentures, bonds or other securities sold by that person for money;
- all of the lease obligations that are capitalized on the books of that person in accordance with generally accepted accounting principles;
- all indebtedness of others of the kinds described in the first two bullet points above and all lease obligations of others of the kind described in the third bullet point above that the person, in any manner, assumes or guarantees or that the person in effect guarantees through an agreement to purchase, whether that agreement is contingent or otherwise; and
- all renewals, extensions or refundings of indebtedness of the kinds described in the first, second or fourth bullet point above and all renewals or extensions of leases of the kinds described in the third or fourth bullet point above;

unless, in the case of any particular indebtedness, renewal, extension or refunding, the instrument creating or evidencing it or the assumption or guarantee relating to it expressly provides that such indebtedness, renewal, extension or refunding is not superior in right of payment to the subordinated debt securities. Our senior debt securities constitute senior indebtedness for purposes of the subordinated indenture.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock is intended as a summary only and therefore is not a complete description of our capital stock. This description is based upon, and is qualified by reference to, our certificate of incorporation, our by-laws and applicable provisions of Delaware corporate law. You should read our certificate of incorporation and by-laws, which are filed as exhibits to the registration statement of which this prospectus forms a part, for the provisions that are important to you.

Our authorized capital stock consists of 200,000,000 shares of our common stock, $0.001 par value per share, and 5,000,000 shares of our preferred stock, $0.001 par value per share. As of July 31, 2018, we had issued and outstanding 36,198,436 shares of our common stock, and no shares of preferred stock were outstanding.

Common Stock

Annual Meeting. Annual meetings of our stockholders are held on the date designated in accordance with our by-laws. Written notice must be mailed to each stockholder entitled to vote not less than ten nor more than 60 days before the date of the meeting. The presence in person or by proxy of the holders of record of a majority of our issued and outstanding shares entitled to vote at such meeting constitutes a quorum for the transaction of business at meetings of the stockholders. Special meetings of the stockholders may be called for any purpose by only the board of directors, the Chairman of the board of directors or the Chief Executive Officer. Except as may be otherwise provided by applicable law, our certificate of incorporation or our by-laws, all elections of directors shall be decided by a plurality of the votes cast by the stockholders entitled to vote on the election, and all other questions shall be decided by the vote of the holders of shares of stock having a majority in voting power of the votes cast by the holders of all of the shares of stock present or represented at the meeting and voting affirmatively or negatively on such matter at a duly held meeting of stockholders at which a quorum is present.

Voting Rights. Each holder of common stock is entitled to one vote for each share held of record on all matters to be voted upon by stockholders.

Dividends. Subject to the rights, powers and preferences of any outstanding preferred stock, and except as provided by law or in our certificate of incorporation, dividends may be declared and paid or set aside for payment on the common stock out of legally available assets or funds when and as declared by the board of directors.

Liquidation and Dissolution. Subject to the rights, powers and preferences of any outstanding preferred stock, in the event of our liquidation or dissolution, our net assets will be distributed pro rata to the holders of our common stock.

Other Rights. Holders of the common stock have no right to:

- convert the stock into any other security;
- have the stock redeemed;
- purchase additional stock; or
- maintain their proportionate ownership interest.

The common stock does not have cumulative voting rights. Holders of shares of the common stock are not required to make additional capital contributions.

Transfer Agent and Registrar. Computershare Trust Company, N.A. is transfer agent and registrar for the common stock.

Preferred Stock

We are authorized to issue "blank check" preferred stock, which may be issued in one or more series upon authorization of our board of directors. Our board of directors is authorized to fix the designations, powers, preferences and the relative, participating, optional or other special rights and any qualifications, limitations and restrictions of the shares of each series of preferred stock. The authorized shares of our preferred stock are available for issuance without further action by our stockholders, unless such action is required by applicable law or the rules of any stock exchange on which our securities may be listed. If the approval of our stockholders is not required for the issuance of shares of our preferred stock, our board may determine not to seek stockholder approval. The specific terms of any series of preferred stock offered pursuant to this prospectus will be described in the prospectus supplement relating to that series of preferred stock.

A series of our preferred stock could, depending on the terms of such series, impede the completion of a merger, tender offer or other takeover attempt. Our board of directors will make any determination to issue preferred shares based upon its judgment as to the best interests of our stockholders. Our directors, in so acting, could issue preferred stock having terms that could discourage an acquisition attempt through which an acquirer may be able to change the composition of our board of directors, including a tender offer or other transaction that some, or a majority, of our stockholders might believe to be in their best interests or in which stockholders might receive a premium for their stock over the then-current market price of the stock.

The preferred stock has the terms described below unless otherwise provided in the prospectus supplement relating to a particular series of preferred stock. You should read the prospectus supplement relating to the particular series of preferred stock being offered for specific terms, including:

- the designation and stated value per share of the preferred stock and the number of shares offered;
- the amount of liquidation preference per share;
- the price at which the preferred stock will be issued;
- the dividend rate, or method of calculation of dividends, the dates on which dividends will be payable, whether dividends will be cumulative or noncumulative and, if cumulative, the dates from which dividends will commence to accumulate;
- any redemption or sinking fund provisions;
- if other than the currency of the United States, the currency or currencies including composite currencies in which the preferred stock is denominated and/or in which payments will or may be payable;
- any conversion provisions;
- whether we have elected to offer depositary shares as described under "Description of Depositary Shares;" and
- any other rights, preferences, privileges, limitations and restrictions on the preferred stock.

The preferred stock will, when issued, be fully paid and non-assessable. Unless otherwise specified in the prospectus supplement, each series of preferred stock will rank equally as to dividends and liquidation rights in all respects with each other series of preferred stock. The rights of holders of shares of each series of preferred stock will be subordinate to those of our general creditors.

As described under "Description of Depositary Shares," we may, at our option, with respect to any series of preferred stock, elect to offer fractional interests in shares of preferred stock, and provide for

the issuance of depositary receipts representing depositary shares, each of which will represent a fractional interest in a share of the series of preferred stock. The fractional interest will be specified in the prospectus supplement relating to a particular series of preferred stock.

Rank. Unless otherwise specified in the prospectus supplement, the preferred stock will, with respect to dividend rights and rights upon our liquidation, dissolution or winding up of our affairs, rank:

- senior to our common stock and to all equity securities ranking junior to such preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs;
- on a parity with all equity securities issued by us, the terms of which specifically provide that such equity securities rank on a parity with the preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs; and
- junior to all equity securities issued by us, the terms of which specifically provide that such equity securities rank senior to the preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs.

The term "equity securities" does not include convertible debt securities.

Dividends. Holders of the preferred stock of each series will be entitled to receive, when, as and if declared by our board of directors, cash dividends at such rates and on such dates described in the prospectus supplement. Different series of preferred stock may be entitled to dividends at different rates or based on different methods of calculation. The dividend rate may be fixed or variable or both. Dividends will be payable to the holders of record as they appear on our stock books on record dates fixed by our board of directors, as specified in the applicable prospectus supplement.

Dividends on any series of preferred stock may be cumulative or noncumulative, as described in the applicable prospectus supplement. If our board of directors does not declare a dividend payable on a dividend payment date on any series of noncumulative preferred stock, then the holders of that noncumulative preferred stock will have no right to receive a dividend for that dividend payment date, and we will have no obligation to pay the dividend accrued for that period, whether or not dividends on that series are declared payable on any future dividend payment dates. Dividends on any series of cumulative preferred stock will accrue from the date we initially issue shares of such series or such other date specified in the applicable prospectus supplement.

No dividends may be declared or paid or funds set apart for the payment of any dividends on any parity securities unless full dividends have been paid or set apart for payment on the preferred stock. If full dividends are not paid, the preferred stock will share dividends pro rata with the parity securities.

No dividends may be declared or paid or funds set apart for the payment of dividends on any junior securities unless full dividends for all dividend periods terminating on or prior to the date of the declaration or payment will have been paid or declared and a sum sufficient for the payment set apart for payment on the preferred stock.

Liquidation Preference. Upon any voluntary or involuntary liquidation, dissolution or winding up of our affairs, then, before we make any distribution or payment to the holders of any common stock or any other class or series of our capital stock ranking junior to the preferred stock in the distribution of assets upon any liquidation, dissolution or winding up of our affairs, the holders of each series of preferred stock shall be entitled to receive out of assets legally available for distribution to stockholders, liquidating distributions in the amount of the liquidation preference per share set forth in the prospectus supplement, plus any accrued and unpaid dividends thereon. Such dividends will not include any accumulation in respect of unpaid noncumulative dividends for prior dividend periods.

Unless otherwise specified in the prospectus supplement, after payment of the full amount of their liquidating distributions, the holders of preferred stock will have no right or claim to any of our remaining assets. Upon any such voluntary or involuntary liquidation, dissolution or winding up, if our available assets are insufficient to pay the amount of the liquidating distributions on all outstanding preferred stock and the corresponding amounts payable on all other classes or series of our capital stock ranking on parity with the preferred stock and all other such classes or series of shares of capital stock ranking on parity with the preferred stock in the distribution of assets, then the holders of the preferred stock and all other such classes or series of capital stock will share ratably in any such distribution of assets in proportion to the full liquidating distributions to which they would otherwise be entitled.

Upon any such liquidation, dissolution or winding up and if we have made liquidating distributions in full to all holders of preferred stock, we will distribute our remaining assets among the holders of any other classes or series of capital stock ranking junior to the preferred stock according to their respective rights and preferences and, in each case, according to their respective number of shares. For such purposes, our consolidation or merger with or into any other corporation, trust or entity, or the sale, lease or conveyance of all or substantially all of our property or assets will not be deemed to constitute a liquidation, dissolution or winding up of our affairs.

Redemption. If so provided in the applicable prospectus supplement, the preferred stock will be subject to mandatory redemption or redemption at our option, as a whole or in part, in each case upon the terms, at the times and at the redemption prices set forth in such prospectus supplement.

The prospectus supplement relating to a series of preferred stock that is subject to mandatory redemption will specify the number of shares of preferred stock that shall be redeemed by us in each year commencing after a date to be specified, at a redemption price per share to be specified, together with an amount equal to all accrued and unpaid dividends thereon to the date of redemption. Unless the shares have a cumulative dividend, such accrued dividends will not include any accumulation in respect of unpaid dividends for prior dividend periods. We may pay the redemption price in cash or other property, as specified in the applicable prospectus supplement. If the redemption price for preferred stock of any series is payable only from the net proceeds of the issuance of shares of our capital stock, the terms of such preferred stock may provide that, if no such shares of our capital stock shall have been issued or to the extent the net proceeds from any issuance are insufficient to pay in full the aggregate redemption price then due, such preferred stock shall automatically and mandatorily be converted into the applicable shares of our capital stock pursuant to conversion provisions specified in the applicable prospectus supplement. Notwithstanding the foregoing, we will not redeem any preferred stock of a series unless:

- if that series of preferred stock has a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full cumulative dividends on the preferred stock for all past dividend periods and the then current dividend period; or

- if such series of preferred stock does not have a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full dividends for the then current dividend period.

In addition, we will not acquire any preferred stock of a series unless:

- if that series of preferred stock has a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full cumulative dividends on all outstanding shares of such series of preferred stock for all past dividend periods and the then current dividend period; or

- if that series of preferred stock does not have a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full dividends on the preferred stock of such series for the then current dividend period.

However, at any time we may purchase or acquire preferred stock of that series (1) pursuant to a purchase or exchange offer made on the same terms to holders of all outstanding preferred stock of such series or (2) by conversion into or exchange for shares of our capital stock ranking junior to the preferred stock of such series as to dividends and upon liquidation.

If fewer than all of the outstanding shares of preferred stock of any series are to be redeemed, we will determine the number of shares that may be redeemed pro rata from the holders of record of such shares in proportion to the number of such shares held or for which redemption is requested by such holder or by any other equitable manner that we determine. Such determination will reflect adjustments to avoid redemption of fractional shares.

Unless otherwise specified in the prospectus supplement, we will mail notice of redemption at least 30 days but not more than 60 days before the redemption date to each holder of record of preferred stock to be redeemed at the address shown on our stock transfer books. Each notice shall state:

- the redemption date;
- the number of shares and series of preferred stock to be redeemed;
- the redemption price;
- the place or places where certificates for such preferred stock are to be surrendered for payment of the redemption price;
- that dividends on the shares to be redeemed will cease to accrue on such redemption date;
- the date on which the holder's conversion rights, if any, as to such shares shall terminate; and
- the specific number of shares to be redeemed from each such holder if fewer than all the shares of any series are to be redeemed.

If notice of redemption has been given and we have set aside the funds necessary for such redemption in trust for the benefit of the holders of any shares called for redemption, then from and after the redemption date, dividends will cease to accrue on such shares, and all rights of the holders of such shares will terminate, except the right to receive the redemption price.

Voting Rights. Holders of preferred stock will not have any voting rights, except as required by law or as indicated in the applicable prospectus supplement.

Unless otherwise provided for under the terms of any series of preferred stock, no consent or vote of the holders of shares of preferred stock or any series thereof shall be required for any amendment to our certificate of incorporation that would increase the number of authorized shares of preferred stock or the number of authorized shares of any series thereof or decrease the number of authorized shares of preferred stock or the number of authorized shares of any series thereof (but not below the number of authorized shares of preferred stock or such series, as the case may be, then outstanding).

Conversion Rights. The terms and conditions, if any, upon which any series of preferred stock is convertible into our common stock will be set forth in the applicable prospectus supplement relating thereto. Such terms will include the number of shares of common stock into which the shares of preferred stock are convertible, the conversion price, rate or manner of calculation thereof, the conversion period, provisions as to whether conversion will be at our option or at the option of the holders of the preferred stock, the events requiring an adjustment of the conversion price and provisions affecting conversion in the event of the redemption.

Transfer Agent and Registrar. The transfer agent and registrar for the preferred stock will be set forth in the applicable prospectus supplement.

Provisions of Our Certificate of Incorporation and By-laws and Delaware Law That May Have Anti-Takeover Effects

Staggered Board; Removal of Directors. Our certificate of incorporation and our bylaws divide our board of directors into three classes with staggered three-year terms. In addition, our certificate of incorporation and our bylaws provide that directors may be removed only for cause and only by the affirmative vote of the holders of 75% of our shares of capital stock present in person or by proxy and entitled to vote. Under our certificate of incorporation and bylaws, any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office. Furthermore, our certificate of incorporation provides that the authorized number of directors may be changed only by the resolution of our board of directors. The classification of our board of directors and the limitations on the ability of our stockholders to remove directors, change the authorized number of directors and fill vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Stockholder Action; Special Meeting of Stockholders; Advance Notice Requirements for Stockholder Proposals and Director Nominations. Our certificate of incorporation and our bylaws provide that any action required or permitted to be taken by our stockholders at an annual meeting or special meeting of stockholders may only be taken if it is properly brought before such meeting and may not be taken by written action in lieu of a meeting. Our certificate of incorporation and our bylaws also provide that, except as otherwise required by law, special meetings of the stockholders can only be called by the chairman of our board of directors, our chief executive officer or our board of directors. In addition, our bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to our board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors, or by a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities. These provisions also could discourage a third party from making a tender offer for our common stock, because even if it acquired a majority of our outstanding voting stock, it would be able to take action as a stockholder, such as electing new directors or approving a merger, only at a duly called stockholders meeting and not by written consent.

Super-Majority Voting. The General Corporation Law of the State of Delaware, which we refer to as the DGCL, provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our bylaws may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described above.

Delaware Business Combination Statute. Section 203 of the DGCL is applicable to us. Section 203 of the DGCL restricts some types of transactions and business combinations between a corporation and

a 15% stockholder. A 15% stockholder is generally considered by Section 203 to be a person owning 15% or more of the corporation's outstanding voting stock. Section 203 refers to a 15% stockholder as an "interested stockholder." Section 203 restricts these transactions for a period of three years from the date the stockholder acquires 15% or more of our outstanding voting stock. With some exceptions, unless the transaction is approved by the board of directors and the holders of at least two-thirds of the outstanding voting stock of the corporation, Section 203 prohibits significant business transactions such as:

- a merger with, disposition of significant assets to or receipt of disproportionate financial benefits by the interested stockholder, and
- any other transaction that would increase the interested stockholder's proportionate ownership of any class or series of our capital stock.

The shares held by the interested stockholder are not counted as outstanding when calculating the two-thirds of the outstanding voting stock needed for approval.

The prohibition against these transactions does not apply if:

- prior to the time that any stockholder became an interested stockholder, the board of directors approved either the business combination or the transaction in which such stockholder acquired 15% or more of our outstanding voting stock, or
- the interested stockholder owns at least 85% of our outstanding voting stock as a result of a transaction in which such stockholder acquired 15% or more of our outstanding voting stock. Shares held by persons who are both directors and officers or by some types of employee stock plans are not counted as outstanding when making this calculation.

Directors' Liability

Our certificate of incorporation limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the Delaware General Corporation Law and provides that no director will have personal liability to us or to our stockholders for monetary damages for breach of fiduciary duty or other duty as a director. However, these provisions do not eliminate or limit the liability of any of our directors:

- for any breach of the director's duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law;
- for voting or assenting to unlawful payments of dividends, stock repurchases or other distributions; or
- for any transaction from which the director derived an improper personal benefit.

Any amendment to or repeal of these provisions will not eliminate or reduce the effect of these provisions in respect of any act, omission or claim that occurred or arose prior to such amendment or repeal. If the Delaware General Corporation Law is amended to provide for further limitations on the personal liability of directors of corporations, then the personal liability of our directors will be further limited to the greatest extent permitted by the Delaware General Corporation Law.

Our certificate of incorporation provides that we must indemnify our directors and officers and we must advance expenses, including attorneys' fees, to our directors and officers in connection with legal proceedings, subject to very limited exceptions.

We maintain a general liability insurance policy that covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers. In

addition, we have entered into indemnification agreements with our directors and executive officers. These indemnification agreements may require us, among other things, to indemnify each such director or executive officer, as applicable, for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by him or her in any action or proceeding arising out of his or her service as one of our directors or executive officers, as applicable.

Certain of our non-employee directors may, through their relationships with their employers, be insured or indemnified against certain liabilities incurred in their capacity as members of our board of directors.

DESCRIPTION OF DEPOSITARY SHARES

General

We may, at our option, elect to offer fractional shares of preferred stock, which we call depositary shares, rather than full shares of preferred stock. If we do, we will issue to the public receipts, called depositary receipts, for depositary shares, each of which will represent a fraction, to be described in the applicable prospectus supplement, of a share of a particular series of preferred stock. Unless otherwise provided in the prospectus supplement, each owner of a depositary share will be entitled, in proportion to the applicable fractional interest in a share of preferred stock represented by the depositary share, to all the rights and preferences of the preferred stock represented by the depositary share. Those rights include dividend, voting, redemption, conversion and liquidation rights.

The shares of preferred stock underlying the depositary shares will be deposited with a bank or trust company selected by us to act as depositary under a deposit agreement between us, the depositary and the holders of the depositary receipts. The depositary will be the transfer agent, registrar and dividend disbursing agent for the depositary shares.

The depositary shares will be evidenced by depositary receipts issued pursuant to the deposit agreement. Holders of depositary receipts agree to be bound by the deposit agreement, which requires holders to take certain actions such as filing proof of residence and paying certain charges.

The summary of terms of the depositary shares contained in this prospectus is not a complete description of the terms of the depositary shares. You should refer to the form of the deposit agreement, our certificate of incorporation and the certificate of designation for the applicable series of preferred stock that are, or will be, filed with the SEC.

Dividends and Other Distributions

The depositary will distribute all cash dividends or other cash distributions, if any, received in respect of the preferred stock underlying the depositary shares to the record holders of depositary shares in proportion to the numbers of depositary shares owned by those holders on the relevant record date. The relevant record date for depositary shares will be the same date as the record date for the underlying preferred stock.

If there is a distribution other than in cash, the depositary will distribute property (including securities) received by it to the record holders of depositary shares, unless the depositary determines that it is not feasible to make the distribution. If this occurs, the depositary may, with our approval, adopt another method for the distribution, including selling the property and distributing the net proceeds from the sale to the holders.

Liquidation Preference

If a series of preferred stock underlying the depositary shares has a liquidation preference, in the event of the voluntary or involuntary liquidation, dissolution or winding up of us, holders of depositary shares will be entitled to receive the fraction of the liquidation preference accorded each share of the applicable series of preferred stock, as set forth in the applicable prospectus supplement.

Withdrawal of Stock

Unless the related depositary shares have been previously called for redemption, upon surrender of the depositary receipts at the office of the depositary, the holder of the depositary shares will be entitled to delivery, at the office of the depositary to or upon his or her order, of the number of whole shares of the preferred stock and any money or other property represented by the depositary shares. If the depositary receipts delivered by the holder evidence a number of depositary shares in excess of the

number of depositary shares representing the number of whole shares of preferred stock to be withdrawn, the depositary will deliver to the holder at the same time a new depositary receipt evidencing the excess number of depositary shares. In no event will the depositary deliver fractional shares of preferred stock upon surrender of depositary receipts. Holders of preferred stock thus withdrawn may not thereafter deposit those shares under the deposit agreement or receive depositary receipts evidencing depositary shares therefor.

Redemption of Depositary Shares

Whenever we redeem shares of preferred stock held by the depositary, the depositary will redeem as of the same redemption date the number of depositary shares representing shares of the preferred stock so redeemed, so long as we have paid in full to the depositary the redemption price of the preferred stock to be redeemed plus an amount equal to any accumulated and unpaid dividends on the preferred stock to the date fixed for redemption. The redemption price per depositary share will be equal to the redemption price and any other amounts per share payable on the preferred stock multiplied by the fraction of a share of preferred stock represented by one depositary share. If less than all the depositary shares are to be redeemed, the depositary shares to be redeemed will be selected by lot or pro rata or by any other equitable method as may be determined by the depositary.

After the date fixed for redemption, depositary shares called for redemption will no longer be deemed to be outstanding and all rights of the holders of depositary shares will cease, except the right to receive the monies payable upon redemption and any money or other property to which the holders of the depositary shares were entitled upon redemption upon surrender to the depositary of the depositary receipts evidencing the depositary shares.

Voting the Preferred Stock

Upon receipt of notice of any meeting at which the holders of the preferred stock are entitled to vote, the depositary will mail the information contained in the notice of meeting to the record holders of the depositary receipts relating to that preferred stock. The record date for the depositary receipts relating to the preferred stock will be the same date as the record date for the preferred stock. Each record holder of the depositary shares on the record date will be entitled to instruct the depositary as to the exercise of the voting rights pertaining to the number of shares of preferred stock represented by that holder's depositary shares. The depositary will endeavor, insofar as practicable, to vote the number of shares of preferred stock represented by the depositary shares in accordance with those instructions, and we will agree to take all action that may be deemed necessary by the depositary in order to enable the depositary to do so. The depositary will not vote any shares of preferred stock except to the extent it receives specific instructions from the holders of depositary shares representing that number of shares of preferred stock.

Charges of Depositary

We will pay all transfer and other taxes and governmental charges arising solely from the existence of the depositary arrangements. We will pay charges of the depositary in connection with the initial deposit of the preferred stock and any redemption of the preferred stock. Holders of depositary receipts will pay transfer, income and other taxes and governmental charges and such other charges (including those in connection with the receipt and distribution of dividends, the sale or exercise of rights, the withdrawal of the preferred stock and the transferring, splitting or grouping of depositary receipts) as are expressly provided in the deposit agreement to be for their accounts. If these charges have not been paid by the holders of depositary receipts, the depositary may refuse to transfer depositary shares, withhold dividends and distributions and sell the depositary shares evidenced by the depositary receipt.

Amendment and Termination of the Deposit Agreement

The form of depositary receipt evidencing the depositary shares and any provision of the deposit agreement may be amended by agreement between us and the depositary. However, any amendment that materially and adversely alters the rights of the holders of depositary shares, other than fee changes, will not be effective unless the amendment has been approved by the holders of a majority of the outstanding depositary shares. The deposit agreement may be terminated by the depositary or us only if:

- all outstanding depositary shares have been redeemed; or
- there has been a final distribution of the preferred stock in connection with our dissolution and such distribution has been made to all the holders of depositary shares.

Resignation and Removal of Depositary

The depositary may resign at any time by delivering to us notice of its election to do so, and we may remove the depositary at any time. Any resignation or removal of the depositary will take effect upon our appointment of a successor depositary and its acceptance of such appointment. The successor depositary must be appointed within 60 days after delivery of the notice of resignation or removal and must be a bank or trust company having its principal office in the United States and having the requisite combined capital and surplus as set forth in the applicable agreement.

Notices

The depositary will forward to holders of depositary receipts all notices, reports and other communications, including proxy solicitation materials received from us, that are delivered to the depositary and that we are required to furnish to the holders of the preferred stock. In addition, the depositary will make available for inspection by holders of depositary receipts at the principal office of the depositary, and at such other places as it may from time to time deem advisable, any reports and communications we deliver to the depositary as the holder of preferred stock.

Limitation of Liability

Neither we nor the depositary will be liable if either we or it is prevented or delayed by law or any circumstance beyond its control in performing its obligations. Our obligations and those of the depositary will be limited to performance in good faith of our and their duties thereunder. We and the depositary will not be obligated to prosecute or defend any legal proceeding in respect of any depositary shares or preferred stock unless satisfactory indemnity is furnished. We and the depositary may rely upon written advice of counsel or accountants, on information provided by persons presenting preferred stock for deposit, holders of depositary receipts or other persons believed to be competent to give such information and on documents believed to be genuine and to have been signed or presented by the proper party or parties.

DESCRIPTION OF UNITS

We may issue units comprised of one or more of the other securities that may be offered under this prospectus, in any combination. The following, together with the additional information we may include in the applicable prospectus supplement, summarizes the material terms and provisions of the units that we may offer under this prospectus. While the terms summarized below will apply generally to any units we may offer, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement.

Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately at any time, or at any time before a specified date.

Any applicable prospectus supplement will describe:

- the material terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any material provisions relating to the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and
- any material provisions of the governing unit agreement that differ from those described above.

DESCRIPTION OF WARRANTS

We may issue warrants to purchase common stock, preferred stock, depositary shares or debt securities. We may offer warrants separately or together with one or more additional warrants, common stock, preferred stock, depositary shares or debt securities, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. If we issue warrants as part of a unit, the accompanying prospectus supplement will specify whether those warrants may be separated from the other securities in the unit prior to the expiration date of the warrants. The applicable prospectus supplement will also describe the following terms of any warrants:

- the specific designation and aggregate number of, and the offering price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;
- whether the warrants are to be sold separately or with other securities as parts of units;
- whether the warrants will be issued in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
- the designation and terms of any equity securities purchasable upon exercise of the warrants;
- the designation, aggregate principal amount, currency and terms of any debt securities that may be purchased upon exercise of the warrants;
- if applicable, the designation and terms of the preferred stock or depositary shares with which the warrants are issued and the number of warrants issued with each security;
- if applicable, the date from and after which any warrants issued as part of a unit and the related debt securities, preferred stock, depositary shares or common stock will be separately transferable;
- the number of shares of common stock, preferred stock or depositary shares purchasable upon exercise of a warrant and the price at which those shares may be purchased;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- the anti-dilution provisions of, and other provisions for changes to or adjustment in the exercise price of, the warrants, if any;
- any redemption or call provisions; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange or exercise of the warrants.

FORMS OF SECURITIES

Each debt security, depositary share, unit and warrant will be represented either by a certificate issued in definitive form to a particular investor or by one or more global securities representing the entire issuance of securities. Unless the applicable prospectus supplement provides otherwise, certificated securities in definitive form and global securities will be issued in registered form. Definitive securities name you or your nominee as the owner of the security, and in order to transfer or exchange these securities or to receive payments other than interest or other interim payments, you or your nominee must physically deliver the securities to the trustee, registrar, paying agent or other agent, as applicable. Global securities name a depositary or its nominee as the owner of the debt securities, depositary shares, units or warrants represented by these global securities. The depositary maintains a computerized system that will reflect each investor's beneficial ownership of the securities through an account maintained by the investor with its broker/dealer, bank, trust company or other representative, as we explain more fully below.

Global Securities

We may issue the debt securities, depositary shares, units and warrants in the form of one or more fully registered global securities that will be deposited with a depositary or its nominee identified in the applicable prospectus supplement and registered in the name of that depositary or nominee. In those cases, one or more global securities will be issued in a denomination or aggregate denominations equal to the portion of the aggregate principal or face amount of the securities to be represented by global securities. Unless and until it is exchanged in whole for securities in definitive registered form, a global security may not be transferred except as a whole by and among the depositary for the global security, the nominees of the depositary or any successors of the depositary or those nominees.

If not described below, any specific terms of the depositary arrangement with respect to any securities to be represented by a global security will be described in the prospectus supplement relating to those securities. We anticipate that the following provisions will apply to all depositary arrangements.

Ownership of beneficial interests in a global security will be limited to persons, called participants, that have accounts with the depositary or persons that may hold interests through participants. Upon the issuance of a global security, the depositary will credit, on its book-entry registration and transfer system, the participants' accounts with the respective principal or face amounts of the securities beneficially owned by the participants. Any dealers, underwriters or agents participating in the distribution of the securities will designate the accounts to be credited. Ownership of beneficial interests in a global security will be shown on, and the transfer of ownership interests will be effected only through, records maintained by the depositary, with respect to interests of participants, and on the records of participants, with respect to interests of persons holding through participants. The laws of some states may require that some purchasers of securities take physical delivery of these securities in definitive form. These laws may impair your ability to own, transfer or pledge beneficial interests in global securities.

So long as the depositary, or its nominee, is the registered owner of a global security, that depositary or its nominee, as the case may be, will be considered the sole owner or holder of the securities represented by the global security for all purposes under the applicable indenture, deposit agreement, warrant agreement or unit agreement. Except as described below, owners of beneficial interests in a global security will not be entitled to have the securities represented by the global security registered in their names, will not receive or be entitled to receive physical delivery of the securities in definitive form and will not be considered the owners or holders of the securities under the applicable indenture, deposit agreement, unit agreement or warrant agreement. Accordingly, each person owning a beneficial interest in a global security must rely on the procedures of the depositary for that global security and, if that person is not a participant, on the procedures of the participant through which the

person owns its interest, to exercise any rights of a holder under the applicable indenture, deposit agreement, unit agreement or warrant agreement. We understand that under existing industry practices, if we request any action of holders or if an owner of a beneficial interest in a global security desires to give or take any action that a holder is entitled to give or take under the applicable indenture, deposit agreement, unit agreement or warrant agreement, the depositary for the global security would authorize the participants holding the relevant beneficial interests to give or take that action, and the participants would authorize beneficial owners owning through them to give or take that action or would otherwise act upon the instructions of beneficial owners holding through them.

Principal, premium, if any, and interest payments on debt securities, and any payments to holders with respect to depositary shares, warrants or units, represented by a global security registered in the name of a depositary or its nominee will be made to the depositary or its nominee, as the case may be, as the registered owner of the global security. None of us, or any trustee, warrant agent, unit agent or other agent of ours, or any agent of any trustee, warrant agent or unit agent will have any responsibility or liability for any aspect of the records relating to payments made on account of beneficial ownership interests in the global security or for maintaining, supervising or reviewing any records relating to those beneficial ownership interests.

We expect that the depositary for any of the securities represented by a global security, upon receipt of any payment to holders of principal, premium, interest or other distribution of underlying securities or other property on that registered global security, will immediately credit participants' accounts in amounts proportionate to their respective beneficial interests in that global security as shown on the records of the depositary. We also expect that payments by participants to owners of beneficial interests in a global security held through participants will be governed by standing customer instructions and customary practices, as is now the case with the securities held for the accounts of customers or registered in "street name," and will be the responsibility of those participants.

If the depositary for any of the securities represented by a global security is at any time unwilling or unable to continue as depositary or ceases to be a clearing agency registered under the Exchange Act, and a successor depositary registered as a clearing agency under the Exchange Act is not appointed by us within 90 days, we will issue securities in definitive form in exchange for the global security that had been held by the depositary. Any securities issued in definitive form in exchange for a global security will be registered in the name or names that the depositary gives to the relevant trustee, warrant agent, unit agent or other relevant agent of ours or theirs. It is expected that the depositary's instructions will be based upon directions received by the depositary from participants with respect to ownership of beneficial interests in the global security that had been held by the depositary.

PLAN OF DISTRIBUTION

We may sell securities:

- through underwriters;
- through dealers;
- through agents;
- directly to purchasers; or
- through a combination of any of these methods of sale.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing security holders. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

We may directly solicit offers to purchase securities, or agents may be designated to solicit such offers. We will, in the prospectus supplement relating to such offering, name any agent that could be viewed as an underwriter under the Securities Act, and describe any commissions that we must pay. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis.

The distribution of the securities may be effected from time to time in one or more transactions:

- at a fixed price, or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

- the name of the agent or any underwriters;
- the public offering or purchase price and the proceeds we will receive from the sale of the securities;
- any discounts and commissions to be allowed or re-allowed or paid to the agent or underwriters;
- all other items constituting underwriting compensation;
- any discounts and commissions to be allowed or re-allowed or paid to dealers; and
- any exchanges on which the securities will be listed.

If any underwriters or agents are utilized in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

If a dealer is utilized in the sale of the securities in respect of which this prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

If we offer securities in a subscription rights offering to our existing security holders, we may enter into a standby underwriting agreement with dealers, acting as standby underwriters. We may pay the standby underwriters a commitment fee for the securities they commit to purchase on a standby basis. If we do not enter into a standby underwriting arrangement, we may retain a dealer-manager to manage a subscription rights offering for us.

Remarketing firms, agents, underwriters, dealers and other persons may be entitled under agreements which they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and

- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Certain agents, underwriters and dealers, and their associates and affiliates may be customers of, have borrowing relationships with, engage in other transactions with, and/or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may overallot in connection with the offering, creating a short position for their own accounts. In addition, to cover overallotments or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in two business days, unless the parties to any such trade expressly agree otherwise or the securities are sold by us to an underwriter in a firm commitment underwritten offering. The applicable prospectus supplement may provide that the original issue date for your securities may be more than two scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the second business day before the original issue date for

your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than two scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

In compliance with the guidelines of the Financial Industry Regulatory Authority, or FINRA, the aggregate maximum discount, commission or agency fees or other items constituting underwriting compensation to be received by any FINRA member or independent broker-dealer will not exceed 8% of the proceeds from any offering pursuant to this prospectus and any applicable prospectus supplement.

LEGAL MATTERS

Unless the applicable prospectus supplement indicates otherwise, the validity of the securities in respect of which this prospectus is being delivered will be passed upon by Wilmer Cutler Pickering Hale and Dorr LLP.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2017, and the effectiveness of our internal control over financial reporting as of December 31, 2017, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

IVERIC bio, Inc.

Common Stock
Pre-Funded Warrants to Purchase Common Stock

PROSPECTUS SUPPLEMENT

Book-Running Managers

Cowen **Credit Suisse**

Lead-Manager

Wedbush PacGrow

June , 2020