

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

**FORM 10-Q**

(Mark One)

**QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**  
For the quarterly period ended March 31, 2021

Or

**TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**  
For the transition period from to

Commission file number: 001-36080

**IVERIC bio, Inc.**

(Exact name of registrant as specified in its charter)

**Delaware**

(State or other jurisdiction of incorporation or organization)

**20-8185347**

(I.R.S. Employer Identification No.)

**Five Penn Plaza Suite 2372**

**New York, NY**

(Address of principal executive offices)

**10001**

(Zip Code)

**(212) 845-8200**

(Registrant's telephone number, including area code)

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

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

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

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

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

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

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

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

As of April 30, 2021 there were 90,255,116 shares of Common Stock, \$0.001 par value per share, outstanding.

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## FORWARD-LOOKING STATEMENTS

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

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

- the potential benefits of our business plan and strategy to develop our therapeutic and gene therapy product candidates and pursue our collaborative gene therapy sponsored research programs;
- the actual and expected effects of the 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, the work and well-being of our employees, and our financial position;
- our expectations regarding the impact of results from GATHER1, our completed Phase 3 clinical trial evaluating Zimura for the treatment of Geographic Atrophy secondary to age-related macular degeneration, on our business and regulatory strategy, including our plans to pursue further development of Zimura;
- the timing, costs, conduct and outcome of GATHER2, our ongoing 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 GATHER2 clinical trial and any other trials we or a potential collaborator may conduct;
- the timing, costs, conduct and outcome of STAR, our ongoing Phase 2b screening trial evaluating Zimura for the treatment of autosomal recessive Stargardt disease, including expectations regarding the recruitment of additional patients for this trial;
- our plans and expectations for developing Zimura in other indications and pursuing lifecycle improvement programs for Zimura;
- our ability to establish and maintain arrangements and capabilities for the manufacture of our therapeutic and gene therapy product candidates, including scale up and validation of the manufacturing process for Zimura drug substance and securing the supply of Zimura drug product and the polyethylene glycol starting material for our expected needs;
- 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;
- our plans and ability to consummate business development transactions, including potential collaboration or out-licensing opportunities for further development and potential commercialization of our product candidates, and in-licenses or other opportunities to acquire rights to additional product candidates or technologies to treat retinal diseases;
- 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 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 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 and HtrA1 inhibition as potentially relevant mechanisms of action to treat Geographic Atrophy and other forms or stages of age-related macular degeneration, 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;
- 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 personnel and human capital resources;
- our intellectual property position;
- the impact of existing and new governmental laws and regulations; and
- our competitive position.

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

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

This Quarterly Report on Form 10-Q includes 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.

### **Summary of Principal Risk Factors**

*The following is a summary of the principal factors that make an investment in our company speculative or risky. This summary does not address all of the risks and uncertainties that we face. Additional risk and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Additional discussion of the risks summarized in this summary, and other risks that we face, can be found in Part II, Item 1A. Risk Factors section of this Quarterly Report on Form 10-Q, and should be carefully considered, together with other information in this Quarterly Report on Form 10-Q and our other filings with the Securities Exchange Commission, before making an investment decision regarding our common stock. The forward-looking statements discussed above are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.*

1. We are a development-stage company without any approved products. The value of your investment is highly dependent on the success of our research and development programs, which carry numerous risks.

2. We have had a history of operating at significant losses and expect to continue to do so until we can successfully commercialize one or more of our product candidates, if ever. We may never achieve profitability.
3. We will need additional financing in order to finish developing and start commercializing one or more of our product candidates, if approved. Securing financing may be challenging and/or dilutive to our shareholders, and if we are unable to secure financing when needed, we may need to curtail our development programs.
4. The COVID-19 pandemic has adversely affected our business, for example, by impacting the initiation and conduct of our clinical trials, the work of our academic collaborators and contract manufacturing organizations, and aspects of our supply chain. Because of the ongoing and fluid nature of the pandemic, it will continue to affect our business.
5. Drug development is inherently risky with numerous scientific, technical, regulatory and other challenges. A promising drug candidate can fail at any time and for any number of reasons.
6. We are pursuing the development of our product candidates using novel mechanisms of action targeting indications for which there are no approved products. These include, for example, complement inhibition and inhibition of High temperature requirement A serine peptidase 1 protein for geographic atrophy; complement inhibition for autosomal recessive Stargardt disease; and gene therapy for rhodopsin-mediated autosomal dominant retinitis pigmentosa and *BEST1*-related inherited retinal diseases. These approaches carry numerous scientific, regulatory and other risks.
7. We have not had any formal meetings with the U.S. Food or Drug Administration, or FDA, or the European Medicines Agency, or EMA, regarding the results of the GATHER1 trial or our regulatory pathway for Zimura following GATHER1, and regulatory authorities may disagree with the design of or our conclusions from the GATHER1 trial, including our belief that it may serve as one of the two Phase 3 clinical trials required for approval by the FDA and EMA. The results of the GATHER2 trial may not replicate the results of the GATHER1 trial. We may need to conduct additional clinical trials or nonclinical studies for Zimura in order to obtain marketing approval.
8. Gene therapy is a novel area of disease treatment that is subject to numerous risks and uncertainties. We have no prior experience conducting clinical development of a gene therapy product.
9. We may discover safety issues with our product candidates due to known and currently unknown factors, which could hamper their further development.
10. Manufacturing our product candidates, including our gene therapies, is technically complex, expensive and time consuming. We may face issues with scaling up and validating the manufacturing process for Zimura. Issues with manufacturing can derail the further development or commercialization of our product candidates.
11. We face substantial competition from large pharmaceutical companies, smaller biotech companies and others.
12. To commercialize any of our product candidates, if approved, we will need to set up a sales and marketing infrastructure. The success of our commercialization efforts will depend in part on the degree of acceptance of our product candidates by patients, the medical community and payors.
13. We do not have any internal manufacturing facilities and rely heavily on our third-party contract manufacturers. They may have different business priorities than we do and may fail to meet our expectations or follow regulatory requirements, including current good manufacturing practices requirements.
14. We do not have any internal laboratories and rely heavily on our third-party contract research organizations as well as our clinical trial sites and academic collaborators. They may have different priorities than we do and may fail to follow regulatory requirements, including good laboratory practice, good clinical practice and other data integrity requirements.
15. If we choose to pursue a collaboration or out-license for the further development and potential commercialization of any of our product candidates, we may not be able to enter into a collaboration or out-license on favorable terms, or at all. Even if we are able to do so, the collaboration or out-license may not be successful.

16. We rely on patents to protect our proprietary position. We may not obtain the patent rights that we seek and/or we may not be able to exclude our competitors from relevant markets. We may be subject to litigation involving our patents or those of third parties.
17. We are highly dependent on our information security systems and those of third parties we work with. A cybersecurity incident may cause interruptions to the progress of our development programs and operations, financial or regulatory penalties and/or harm to our reputation.
18. We rely on a limited number of employees to conduct our operations, including supervising our outside vendors. The skills needed to advance our research and development programs and plan for eventual commercialization of our product candidates are highly specialized. We plan to hire additional qualified personnel, including commercialization personnel, to support the growth of our business. Hiring these personnel and retaining existing employees may be challenging.
19. We need to satisfy numerous regulatory requirements in order to secure marketing approval and reimbursement approval, if applicable, for any of our product candidates. These requirements differ across jurisdictions. Failure to satisfy and maintain those requirements can preclude us from commercializing our products.
20. We and any commercialization partners are subject to numerous healthcare laws and regulations governing our relationships with patients, healthcare professionals and third-party payors. Failure to comply with these requirements may adversely affect our business.
21. The reimbursement and payment regime for pharmaceutical products in the United States remains in flux, including as a result of the implementation of and litigation involving the Affordable Care Act. There are ongoing, and often bipartisan, efforts to reduce the prices of pharmaceutical products.

#### **USE OF TRADEMARKS**

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

## PART I—FINANCIAL INFORMATION

## Item 1. Financial Statements

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

	March 31, 2021	December 31, 2020
<b>Assets</b>		
Current assets		
Cash and cash equivalents	\$ 29,335	\$ 66,373
Available for sale securities	150,866	143,674
Prepaid expenses and other current assets	5,310	4,791
Income tax receivable	1,765	1,765
Total current assets	187,276	216,603
Property and equipment, net	17	26
Right-of-use asset, net	107	120
Other assets	2	5
Total assets	\$ 187,402	\$ 216,754
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities		
Accrued research and development expenses	\$ 13,132	\$ 12,284
Accounts payable and accrued expenses	6,976	12,792
Lease liability	55	54
Total current liabilities	20,163	25,130
Lease liability, non-current	51	61
Total liabilities	20,214	25,191
Stockholders' equity		
Preferred stock—\$0.001 par value, 5,000,000 shares authorized, no shares issued or outstanding	—	—
Common stock—\$0.001 par value, 200,000,000 shares authorized, 90,169,616 and 90,120,797 shares issued and outstanding at March 31, 2021 and December 31, 2020, respectively	90	90
Additional paid-in capital	758,964	756,543
Accumulated deficit	(591,868)	(565,073)
Accumulated other comprehensive income	2	3
Total stockholders' equity	167,188	191,563
Total liabilities and stockholders' equity	\$ 187,402	\$ 216,754

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

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

	Three Months Ended March 31,	
	2021	2020
Operating expenses:		
Research and development	\$ 18,549	\$ 13,750
General and administrative	8,322	4,998
Total operating expenses	26,871	18,748
Loss from operations	(26,871)	(18,748)
Interest income	77	358
Other income (expense), net	(1)	5
Loss before income tax benefit	(26,795)	(18,385)
Income tax benefit	—	3,309
Net loss	\$ (26,795)	\$ (15,076)
Comprehensive loss	\$ (26,796)	\$ (15,076)
Net loss per common share:		
Basic and diluted	\$ (0.29)	\$ (0.28)
Weighted average common shares outstanding:		
Basic and diluted	93,311	53,426

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



**IVERIC bio, Inc.**

**Condensed Unaudited Consolidated Statements of Stockholders' Equity**

(in thousands)

	Preferred Stock		Common Stock		Additional paid-in capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total
	Shares	Amount	Shares	Amount				
<b>Balance at December 31, 2020</b>	—	\$ —	90,121	\$ 90	\$ 756,543	\$ (565,073)	\$ 3	\$ 191,563
Issuance of common stock under employee stock compensation plans	—	—	49	—	129	—	—	129
Share-based compensation	—	—	—	—	2,292	—	—	2,292
Net loss	—	—	—	—	—	(26,795)	—	(26,795)
Unrealized loss on available for sale securities, net of tax	—	—	—	—	—	—	(1)	(1)
<b>Balance at March 31, 2021</b>	<u>—</u>	<u>\$ —</u>	<u>90,170</u>	<u>\$ 90</u>	<u>\$ 758,964</u>	<u>\$ (591,868)</u>	<u>\$ 2</u>	<u>\$ 167,188</u>
	Preferred Stock		Common Stock		Additional paid-in capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total
	Shares	Amount	Shares	Amount				
<b>Balance at December 31, 2019</b>	—	\$ —	49,627	\$ 50	\$ 597,679	\$ (480,526)	\$ —	\$ 117,203
Issuance of common stock under employee stock compensation plans	—	—	105	—	179	—	—	179
Share-based compensation	—	—	—	—	2,324	—	—	2,324
Net loss	—	—	—	—	—	(15,076)	—	(15,076)
<b>Balance at March 31, 2020</b>	<u>—</u>	<u>\$ —</u>	<u>49,732</u>	<u>\$ 50</u>	<u>\$ 600,182</u>	<u>\$ (495,602)</u>	<u>\$ —</u>	<u>\$ 104,630</u>

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

**IVERIC bio, Inc.**  
**Condensed Unaudited Consolidated Statements of Cash Flows**  
(in thousands)

	<b>Three Months Ended March 31,</b>	
	<b>2021</b>	<b>2020</b>
<b>Operating Activities</b>		
Net loss	\$ (26,795)	\$ (15,076)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation and other expense	13	38
Amortization of premium and discounts on investment securities	395	—
Share-based compensation	2,292	2,324
Changes in operating assets and liabilities:		
Income tax receivable	—	(2,942)
Prepaid expense and other assets	(516)	(140)
Accrued interest receivable	122	—
Accrued research and development expenses	848	1,524
Accounts payable and accrued expenses	(5,816)	(3,254)
Net cash used in operating activities	<u>(29,457)</u>	<u>(17,526)</u>
<b>Investing Activities</b>		
Purchase of marketable securities	(26,710)	—
Maturities of marketable securities	19,000	—
Net cash used in investing activities	<u>(7,710)</u>	<u>—</u>
<b>Financing Activities</b>		
Proceeds from employee stock plan purchases	129	179
Net cash provided by financing activities	129	179
Net decrease in cash and cash equivalents	<u>(37,038)</u>	<u>(17,347)</u>
<b>Cash and cash equivalents</b>		
Beginning of period	66,373	125,699
End of period	<u>\$ 29,335</u>	<u>\$ 108,352</u>

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

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

## 1. Business

### Description of Business and Organization

IVERIC bio, Inc. (the “Company” or “IVERIC”) is a science-driven biopharmaceutical company focused on the discovery and development of novel treatment options for retinal diseases with significant unmet medical needs. The Company is currently developing both therapeutic product candidates for age-related retinal diseases and gene therapy product candidates for orphan inherited retinal diseases (“IRDs”). The Company believes that both therapeutics and gene therapy serve important roles in drug development and providing potential treatment options for patients suffering from retinal diseases.

The Company’s therapeutics portfolio consists of its clinical stage product candidate Zimura® (avacincaptad pegol), a complement C5 inhibitor, and its preclinical product candidate IC-500, a High temperature requirement A serine peptidase 1 protein (“HtrA1”) inhibitor. The Company is currently targeting the following diseases with Zimura:

- Geographic Atrophy (“GA”), which is the advanced stage of age-related macular degeneration (“AMD”), and is characterized by marked thinning or atrophy of retinal tissue, leading to irreversible loss of vision; and
- autosomal recessive Stargardt disease (“STGD1”), which is an orphan inherited condition characterized by progressive damage to the central portion of the retina (the “macula”) and other retinal tissue, leading to loss of vision.

The Company is continuing to recruit and enroll patients in GATHER2, its ongoing Phase 3 clinical trial evaluating the safety and efficacy of Zimura for the treatment of GA secondary to AMD, and expects to complete patient enrollment during the third quarter of 2021. The Company is developing IC-500 for GA secondary to AMD and potentially other age-related retinal diseases.

The Company’s gene therapy portfolio consists of two product candidates in preclinical development (IC-100 and IC-200) and several ongoing collaborative sponsored research programs, each of which uses adeno-associated virus (“AAV”) for gene delivery. These AAV mediated gene therapy programs are targeting the following orphan IRDs:

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

The Company is developing IC-100 for RHO-adRP and IC-200 for *BEST1*-related IRDs.

## 2. Summary of Significant Accounting Policies

The Company’s significant accounting policies are described in Note 2, “Summary of Significant Accounting Policies,” in the notes to the audited consolidated financial statements included in the Company’s Annual Report on Form 10-K (“Annual Report”) for the year ended December 31, 2020 filed with the Securities and Exchange Commission (“SEC”) on March 4, 2021.

### Basis of Presentation and Consolidation

In the opinion of management, the Company’s condensed consolidated financial statements include all adjustments, consisting of normal recurring accruals, necessary for a fair statement of the Company’s financial statements for interim periods in accordance with accounting principles generally accepted in the United States (“U.S. GAAP”). The consolidated financial statements include the accounts of the Company and its subsidiaries. All intercompany balances and transactions have been eliminated in consolidation. The information included in this quarterly report on Form 10-Q should be read in conjunction with the Company’s audited consolidated financial statements and the accompanying notes included in the Annual Report.

The year-end condensed consolidated balance sheet data presented for comparative purposes was derived from the Company's audited financial statements but does not include all disclosures required by U.S. GAAP. The results of operations for the three months ended March 31, 2021 are not necessarily indicative of the operating results for the full year or for any other subsequent interim period.

### **Segment and Geographic Information**

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

### **Use of Estimates**

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

### **Cash and Cash Equivalents**

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

### **Available for Sale Securities**

The Company considers securities with original maturities of greater than 90 days to be available for sale securities. Available for sale securities with original maturities of greater than one year are recorded as non-current assets. Available for sale securities are recorded at fair value and unrealized gains and losses are recorded within other comprehensive income.

On a quarterly basis, the Company reviews the status of each security in an unrealized loss position, to evaluate the existence of potential credit losses. The Company first considers whether it intends to sell, or if it is more likely than not that the Company will be required to sell the security before recovery of its amortized cost basis. If either of the criteria regarding intent or requirement to sell is met, the security's amortized cost basis is written down to fair value through income. For securities that do not meet this criteria, the Company considers a number of factors to determine if the decline in fair value has resulted from credit losses or other factors, including but not limited to: (1) the extent of the decline; (2) changes to the rating of the security by a rating agency; (3) any adverse conditions specific to the security; and (4) other market conditions that may affect the fair value of the security. If this assessment indicates that a credit loss exists and the present value of cash flows expected to be collected is less than the amortized cost basis, an allowance for credit losses is required for the credit loss. Any impairment that has not been recorded through an allowance for credit losses is recognized in other comprehensive income.

### **Financial Instruments**

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

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

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

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

- Level 1—inputs to the valuation methodology are quoted prices (unadjusted) for an identical asset or liability in an active market. The Company's Level 1 assets consist of investments in money market funds and U.S. Treasury securities.
- Level 2—inputs to the valuation methodology include quoted prices for a similar asset or liability in an active market or model-derived valuations in which all significant inputs are observable for substantially the full term of the asset or liability. The Company's Level 2 assets consist of investments in investment-grade corporate debt securities.
- Level 3—inputs to the valuation methodology are unobservable and significant to the fair value measurement of the asset or liability. The Company does not hold any assets that are measured using Level 3 inputs.

### **Concentration of Credit Risk**

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

The Company believes it is not exposed to significant credit risk on its cash, cash equivalents and available for sale securities.

### **Concentration of Suppliers**

The Company historically relied upon a single third-party manufacturer to provide the drug substance for Zimura on a purchase order basis. The Company also historically relied upon a single third-party manufacturer to provide fill/finish services for clinical supplies of Zimura. The Company has engaged one additional third-party manufacturer to provide drug substance for Zimura and one additional third-party manufacturer to provide fill/finish services for clinical supplies of Zimura. In addition, the Company currently relies upon a single third-party supplier to supply on a purchase order basis the polyethylene glycol starting material used to manufacture Zimura. Furthermore, the Company and its contract manufacturers currently rely upon sole-source suppliers of certain raw materials and other specialized components of production used in the manufacture and fill/finish of Zimura. The Company currently relies exclusively upon a single third-party contract manufacturer for IC-100 and IC-200 and also relies on sole-source suppliers for certain starting materials used in the manufacture of such product candidates. The Company currently relies upon a single third-party contract manufacturer to conduct process development, scale-up and GMP manufacture of the drug substance for IC-500 for preclinical toxicology studies and early-stage clinical trials and a single third-party contract manufacturer to conduct formulation development activities for IC-500. If the Company's third-party manufacturers or fill/finish service providers should become unavailable to the Company for any reason, including as a result of capacity constraints, different business objectives, financial difficulties, insolvency or the COVID-19 pandemic, the Company believes that there are a limited number of potential replacement manufacturers, and the Company likely would incur added costs and delays in identifying or qualifying such replacements.

### **Foreign Currency Translation**

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

### **Leases**

The Company determines if an arrangement contains a lease at inception. For arrangements where the Company is the lessee, it recognizes a right-of-use ("ROU") asset and operating lease liability on the Company's Consolidated Balance Sheet. ROU lease assets represent the Company's right to use the underlying asset for the lease term and the lease obligation represents the Company's commitment to make the lease payments arising from the lease. Right-of-use lease assets and obligations are recognized at the commencement date based on the present value of remaining lease payments over the lease term. As the Company's leases do not provide an implicit discount rate, the Company has used an estimated incremental borrowing rate based on the information available at the commencement date in determining the present value of lease payments. ROU lease

asset includes any lease payments made prior to commencement and excludes any lease incentives. The lease term may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. Operating lease expense is recognized on a straight-line basis over the lease term, subject to any changes in the lease or expectations regarding the terms. Variable lease costs such as common area costs and property taxes are expensed as incurred. For all office lease agreements the Company combines lease and nonlease components. Leases with an initial term of 12 months or less are not recorded on the Company's Consolidated Balance Sheet.

### **Property and Equipment**

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

### **Research and Development**

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

- external research and development expenses incurred under arrangements with third parties, such as academic research collaborators, contract research organizations ("CROs") and contract development and manufacturing organizations ("CDMOs") and other vendors for the production and analysis of drug substance and drug product; and
- employee-related expenses for employees dedicated to research and development activities, including salaries, benefits and share-based compensation expense.

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

All research and development expenses are charged to operations as incurred in accordance with ASC 730, *Research and Development*. The Company accounts for non-refundable advance payments for goods and services that will be used in future research and development activities as expenses when the service has been performed or when the goods have been received, rather than when the payment is made.

### **Income Taxes**

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

### **Share-Based Compensation**

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

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

### Stock Options

The Company estimates the fair value of stock options granted to employees, non-employee directors and consultants on the date of grant using the Black-Scholes option-pricing model. The Company's computation of stock-price volatility is based on daily historical volatility during the time period that corresponds to the expected option term. The Company's computation of expected term is determined using the expected term of stock option grants to employees based on an analysis of actual option exercises. The Company utilizes a dividend yield of zero based on the fact that the Company has never paid cash dividends to stockholders and has no current intentions to pay cash dividends. The risk-free interest rate is based on the zero-coupon U.S. Treasury yield at the date of grant for a term equivalent to the expected term of the option.

The weighted-average assumptions used to estimate grant date fair value of stock options using the Black-Scholes option pricing model were as follows for the three month periods ended March 31, 2021 and 2020:

	Three Months Ended March 31,	
	2021	2020
Expected common stock price volatility	113%	115%
Risk-free interest rate	0.39%-0.96%	0.87%-1.34%
Expected term of options (years)	5.3	4.7
Expected dividend yield	—	—

### RSUs

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

### ESPP

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

### Recent Accounting Pronouncements

The Company has evaluated recent accounting pronouncements through the date the financial statements were issued and filed with the SEC and believes that there are none that will have a material impact on the Company's financial statements.

### 3. Common Stock

In June 2020, the Company completed an underwritten public offering in which the Company sold 28,503,220 shares of its common stock, which includes the exercise in full of the underwriters' option to purchase additional shares of the Company's common stock, at a price to the public of \$4.100 per share and at a price to the underwriters of \$3.854 per share. The Company also sold to certain investors in lieu of common stock, pre-funded warrants to purchase 1,914,280 shares of its common stock at a price to the public of \$4.099 per share underlying each pre-funded warrant, and at a price to the underwriters of \$3.853 per share underlying each pre-funded warrant.

Concurrently with the June 2020 public offering, the Company completed a private placement in which the Company sold 8,649,453 shares of its common stock to affiliates of Vivo Capital, LLC and Samsara BioCapital, LP, at a sale price equal to the price to the public in the underwritten public offering.

The net proceeds from the public offering and private placement, after deducting underwriting discounts, underwriting and placement agent commissions and other expenses totaling \$10.1 million, was approximately \$150.1 million.

The Company evaluated the pre-funded warrants for liability or equity classification in accordance with the provisions of ASC 480, *Distinguishing Liabilities from Equity*, and ASC 815-40, *Derivatives and Hedging*. Based on the provisions governing the pre-funded warrants in the applicable agreement, the Company determined that the pre-funded warrants meet the criteria required to be classified as an equity award subject to the guidance in ASC 815-10 and 815-40 and should effectively be treated as outstanding common shares in both basic and diluted earnings per share calculations.

#### 4. Net Loss Per Common Share

Basic and diluted net loss per common share is determined by dividing net loss by the weighted average common shares and pre-funded warrants outstanding during the period. Basic and diluted shares outstanding includes the weighted average effect of the Company's outstanding pre-funded warrants as the exercise of such pre-funded warrants requires nominal consideration to be given for the delivery of the corresponding shares of common stock. As of March 31, 2021, the Company had 3,164,280 pre-funded warrants outstanding, which if exercised, would increase the number of shares of common stock issued and outstanding. For the periods when there is a net loss, shares underlying stock options and RSUs have been excluded from the calculation of diluted net loss per common share because the effect of including such shares would be anti-dilutive. Therefore, the weighted average common shares used to calculate both basic and diluted net loss per common share would be the same.

The following table sets forth the computation of basic and diluted net loss per common share for the periods indicated:

	Three Months Ended March 31,	
	2021	2020
Basic and diluted net loss per common share calculation:		
Net loss	\$ (26,795)	\$ (15,076)
Weighted average common shares outstanding - basic and dilutive	93,311	53,426
Net loss per share of common stock - basic and diluted	\$ (0.29)	\$ (0.28)

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

	Three Months Ended March 31,	
	2021	2020
Stock options outstanding	9,178	6,635
Restricted stock units	2,038	1,401
Total	11,216	8,036

#### 5. Cash, Cash Equivalents and Available for Sale Securities

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at the date of purchase to be cash equivalents. As of March 31, 2021 and December 31, 2020, the Company had cash and cash equivalents of approximately \$29.3 million and \$66.4 million, respectively. Cash and cash equivalents included cash of \$3.3 million at March 31, 2021 and \$8.4 million at December 31, 2020. Cash and cash equivalents at March 31, 2021 and December 31, 2020 included \$26.0 million and \$58.0 million, respectively, of investments in money market funds.

The Company considers securities with original maturities of greater than 90 days at the date of purchase to be available for sale securities. As of March 31, 2021 and December 31, 2020, the Company held available for sale securities of \$150.9 million and \$143.7 million, respectively, all of which have maturities of less than one year.

The Company evaluates securities with unrealized losses, if any, to determine whether the decline in fair value has resulted from credit loss or other factors. The Company has determined that there were no credit losses in fair value of its investments as of March 31, 2021. Factors considered in determining whether a loss resulted from a credit loss or other factors included the length of time and extent to which the investment's fair value has been less than the cost basis, the financial condition and near-term prospects of the investee, the extent of the loss related to credit of the issuer, the expected cash flows from the security, the Company's intent to sell the security, and whether or not the Company will be required to sell the security before the recovery of its amortized cost.

The Company classifies these securities as available for sale. However, the Company has not sold and does not currently intend to sell its investments and the Company believes it is more likely than not that the Company will recover the carrying value of these investments.

The Company believes that its existing cash, cash equivalents and available for sale securities as of March 31, 2021 will be sufficient to fund its currently planned capital expenditure requirements and operating expenses for at least the next 12 months from the filing of this Quarterly Report on Form 10-Q.



Available for sale securities, including carrying value and estimated fair values, are summarized as follows:

	As of March 31, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
U.S. Treasury securities	\$ 45,111	\$ 12	\$ —	\$ 45,123
Corporate debt securities	91,559	2	(12)	91,549
Asset-backed securities	14,194	1	(1)	14,194
Total	\$ 150,864	\$ 15	\$ (13)	\$ 150,866

The Company's available for sale securities are reported at fair value on the Company's balance sheet. Unrealized gains (losses) are reported within other comprehensive income in the statements of comprehensive loss. The cost of securities sold and any realized gains/losses from the sale of available for sale securities are based on the specific identification method. The changes in accumulated other comprehensive income associated with the unrealized gain on available for sale securities during the three months ended March 31, 2021 and 2020, respectively, were as follows:

	Three months ended March 31,	
	2021	2020
Beginning balance	\$ 3	\$ —
Current period changes in fair value before reclassifications, net of tax	(1)	—
Amounts reclassified from accumulated other comprehensive income, net of tax	—	—
Total other comprehensive income	\$ (1)	\$ —
Ending balance	\$ 2	\$ —

## 6. Share-Based Compensation

Pursuant to the evergreen provisions of the Company's 2013 stock incentive plan (the "2013 Plan"), annual increases have resulted in the addition of an aggregate of approximately 13,081,000 additional shares to the 2013 Plan, including for 2021, an increase of approximately 2,542,000 shares. As of March 31, 2021, the Company had approximately 2,874,000 shares available for grant under the 2013 Plan.

In October 2019, the Company's board of directors adopted its 2019 Inducement Stock Incentive Plan (the "2019 Inducement Plan") to reserve initially 1,000,000 shares of its common stock to be used exclusively for grants of awards to individuals who were not previously employees or directors of the Company as a material inducement to such individuals' entry into employment with the Company within Rule 5635(c)(4) of the Nasdaq Listing Rules. The terms and conditions of the 2019 Inducement Plan are substantially similar to those of the 2013 Plan. In March 2020, the Company's board of directors amended the 2019 Inducement Plan to reserve an additional 1,000,000 shares of its common stock for issuance under the plan and in February 2021, the Company's board of directors further amended the 2019 Inducement Plan to reserve an additional 600,000 shares of its common stock for issuance under the plan. As of March 31, 2021, the Company had approximately 891,000 shares available for grant under the 2019 Inducement Plan.

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

	Three Months Ended March 31,	
	2021	2020
Stock options	\$ 1,469	\$ 1,374
Restricted stock units	792	936
Employee stock purchase plan	31	14
Total	\$ 2,292	\$ 2,324

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

	Three Months Ended March 31,	
	2021	2020
Research and development	\$ 1,343	\$ 1,153
General and administrative	949	1,171
<b>Total</b>	<b>\$ 2,292</b>	<b>\$ 2,324</b>

#### Stock Options

A summary of the stock option activity, weighted average exercise prices, options outstanding, exercisable and expected to vest as of March 31, 2021 is as follows (in thousands except weighted average exercise price):

	Number of Shares Underlying Options	Weighted Average Exercise Price
Outstanding, December 31, 2020	8,928	\$ 9.22
Granted	266	\$ 6.38
Exercised	(2)	\$ 3.80
Forfeited	(14)	\$ 4.77
<b>Outstanding, March 31, 2021</b>	<b>9,178</b>	<b>\$ 9.41</b>
Vested and exercisable, March 31, 2021	4,856	\$ 13.22
<b>Vested and expected to vest, March 31, 2021</b>	<b>8,832</b>	<b>\$ 9.58</b>

As of March 31, 2021, there were approximately \$14.3 million of unrecognized compensation costs, net of estimated forfeitures, related to stock awards grants, which are expected to be recognized over a remaining weighted average period of 3.3 years.

#### RSUs

The following table presents a summary of the Company's outstanding RSU awards granted as of March 31, 2021 (in thousands except weighted average grant-date fair value):

	Restricted Stock Units	Weighted Average Grant-Date Fair Value
Outstanding, December 31, 2020	1,958	\$ 6.95
Awarded	112	\$ 6.33
Vested	(22)	\$ 3.83
Forfeited	(10)	\$ 7.50
<b>Outstanding, March 31, 2021</b>	<b>2,038</b>	<b>\$ 7.01</b>
Outstanding, Expected to vest	1,815	\$ 5.31

As of March 31, 2021, there were approximately \$8.5 million of unrecognized compensation costs, net of estimated forfeitures, related to RSUs grants, which are expected to be recognized over a remaining weighted average period of 3.1 years.

#### ESPP

As of March 31, 2021, there were 780,939 shares available for future purchases under the ESPP. There were 24,422 and 43,581 shares issued under the ESPP during the three months ended March 31, 2021 and 2020, respectively. Cash proceeds from ESPP purchases were \$121 thousand and \$42 thousand during the three months ended March 31, 2021 and 2020, respectively.

## 7. Income Taxes

For the three months ended March 31, 2021, the Company recorded no income tax benefit. For the three months ended March 31, 2020, the Company recorded an income tax benefit of \$3.3 million primarily to reflect a settlement of a local tax audit.

In response to the COVID-19 pandemic, the U.S. Congress enacted the Coronavirus Aid, Relief, and Economic Security Act (“CARES Act”) on March 27, 2020. The CARES Act provides numerous tax provisions and other stimulus measures, including the immediate refund of minimum tax credits. The Company has recorded a current tax receivable of approximately \$1.8 million in anticipation of this refund.

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

## 8. Fair Value Measurements

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

The following table presents, for each of the fair value hierarchy levels required under ASC 820, the Company's assets and liabilities that are measured at fair value on a recurring basis as of March 31, 2021:

	Fair Value Measurement Using		
	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
<b>Assets</b>			
Investments in money market funds*	\$ 26,045	\$ —	\$ —
Investments in U.S. Treasury securities	\$ 45,123	\$ —	\$ —
Investments in corporate debt securities	\$ —	\$ 91,549	\$ —
Investments in asset-backed securities	\$ —	\$ 14,194	\$ —

The following table presents, for each of the fair value hierarchy levels required under ASC 820, the Company's assets and liabilities that are measured at fair value on a recurring basis as of December 31, 2020:

	Fair Value Measurement Using		
	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
<b>Assets</b>			
Investments in money market funds*	\$ 58,042	\$ —	\$ —
Investments in U.S. Treasury securities	\$ 54,233	\$ —	\$ —
Investments in corporate debt securities	\$ —	\$ 79,275	\$ —
Investments in asset-backed securities	\$ —	\$ 10,166	\$ —

\* Investments in money market funds are reflected in cash and cash equivalents in the accompanying Consolidated Balance Sheets.

No transfer of assets between Level 1 and Level 2 of the fair value measurement hierarchy occurred during the three months ended March 31, 2021.

## 9. Commitments and Contingencies

### *Zimura - Archemix Corp.*

The Company is party to an agreement with Archemix Corp. (“Archemix”) under which the Company in-licensed rights in certain patents, patent applications and other intellectual property related to Zimura and pursuant to which the Company may be required to pay sublicense fees and make milestone payments (the “C5 License Agreement”). Under the C5 License Agreement, for each anti-C5 aptamer product that the Company may develop under the agreement, including Zimura, the Company is obligated to make additional payments to Archemix of up to an aggregate of \$50.5 million if the Company achieves specified development, clinical and regulatory milestones, with \$24.5 million of such payments relating to a first indication, \$23.5 million of such payments relating to second and third indications and \$2.5 million of such payments relating to sustained delivery applications. Under the C5 License Agreement, the Company is also obligated to make additional payments to Archemix of up to an aggregate of \$22.5 million if the Company achieves specified commercial milestones based on net product sales of all anti-C5 products licensed under the agreement. The Company is also obligated to pay Archemix a double-digit percentage of specified non-royalty payments the Company may receive from any sublicensee of its rights under the C5 License Agreement. The Company is not obligated to pay Archemix a running royalty based on net product sales in connection with the C5 License Agreement.

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

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

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

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

### *miniCEP290 Program - University of Massachusetts*

Under its exclusive license agreement with the University of Massachusetts (“UMass”) for its miniCEP290 program, which targets LCA10, which is associated with mutations in the *CEP290* gene, the Company is obligated to pay UMass up to

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

#### *IC-500 - Former Equityholders of Inception 4*

Under the agreement and plan of merger between the Company and Inception 4, Inc. (“Inception 4”), pursuant to which the Company acquired IC-500 and its other HtrA1 inhibitors (the “Inception 4 Merger Agreement”), the Company is obligated to make payments to the former equityholders of Inception 4 of up to an aggregate of \$105 million, subject to the terms and conditions of the Inception 4 Merger Agreement, if the Company achieves certain specified clinical and regulatory milestones with respect to IC-500 or any other product candidate from its HtrA1 inhibitor program, with \$45 million of such potential payments relating to GA and \$60 million of such potential payments relating to wet AMD. Under the Inception 4 Merger Agreement, the Company does not owe any commercial milestones or royalties based on net sales. The future milestone payments will be payable in the form of shares of the Company’s common stock, calculated based on the price of its common stock over a five-trading day period preceding the achievement of the relevant milestone, unless and until the issuance of such shares would, together with all other shares issued in connection with the acquisition, exceed an overall maximum limit of approximately 7.2 million shares, which is equal to 19.9% of the number of issued and outstanding shares of the Company’s common stock as of the close of business on the business day prior to the closing date of the Inception 4 acquisition, and will be payable in cash thereafter. The Inception 4 Merger Agreement also includes customary indemnification obligations to the former equityholders of Inception 4, including for breaches of the representations and warranties, covenants and agreements of the Company and its subsidiaries (other than Inception 4) in the Inception 4 Merger Agreement.

#### *Employment Contracts*

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

#### *Contract Service Providers*

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

#### *Legal Proceedings*

On January 11, 2017, a putative class action lawsuit was filed against the Company and certain of its current and former executive officers in the United States District Court for the Southern District of New York, captioned Frank Micholle v. IVERIC bio, Inc., et al., No. 1:17-cv-00210. On March 9, 2017, a related putative class action lawsuit was filed against the Company and the same group of its current and former executive officers in the United States District Court for the Southern District of New York, captioned Wasson v. IVERIC bio, Inc., et al., No. 1:17-cv-01758. These cases were consolidated on March 13, 2018. On June 4, 2018, the lead plaintiff filed a consolidated amended complaint (the “CAC”). The CAC purports to be brought on behalf of shareholders who purchased the Company’s common stock between March 2, 2015 and December 12, 2016. The CAC generally alleges that the Company and certain of its officers violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning the results of the Company’s Phase 2b trial and the prospects of the Company’s Phase 3 trials for Fovista in combination with anti-VEGF agents for the treatment of wet AMD. The CAC seeks unspecified damages, attorneys’ fees,

and other costs. The Company and individual defendants filed a motion to dismiss the CAC on July 27, 2018. On September 18, 2019, the court issued an order dismissing some, but not all, of the allegations in the CAC. On November 18, 2019, the Company and the individual defendants filed an answer to the complaint. On June 12, 2020, the lead plaintiff filed a motion for class certification. On August 11, 2020, the defendants filed a notice of non-opposition to lead plaintiff's motion for class certification. On April 22, 2021, the Company and Plaintiff agreed to stay the litigation until 10 days following a mediation scheduled for June 21, 2021. On April 23, 2021, the court approved the stipulation and stayed the action until July 1, 2021.

On August 31, 2018, a shareholder derivative action was filed against current and former members of the Company's Board of Directors and certain current and former officers of the Company in the United States District Court for the Southern District of New York, captioned Luis Pacheco v. David R. Guyer, et al., Case No. 1:18-cv-07999. The complaint, which is based substantially on the facts alleged in the CAC, alleges that the defendants breached their fiduciary duties to the Company and wasted the Company's corporate assets by failing to oversee the Company's business, and also alleges that the defendants were unjustly enriched as a result of the alleged conduct, including through receipt of bonuses, stock options and similar compensation from the Company, and through sales of the Company's stock between March 2, 2015 and December 12, 2016. The complaint purports to seek unspecified damages on the Company's behalf, attorneys' fees, and other costs, as well as an order directing the Company to reform and improve its corporate governance and internal procedures to comply with applicable laws, including submitting certain proposed amendments to the Company's corporate charter, bylaws and corporate governance policies for vote by the Company's stockholders. On December 14, 2018, the Company filed a motion to dismiss the complaint. On September 19, 2019, the court denied its motion to dismiss this complaint. This matter was subsequently referred to a special litigation committee of the Company's board of directors. On February 18, 2020, the Company filed an answer to the complaint. The Company and the plaintiff agreed to stay this litigation while the special litigation committee conducts its investigation. On May 4, 2020, the court approved the stipulation and stayed the litigation through November 1, 2020. By agreement of the parties, the court has since extended the stay through May 22, 2021. The Company also entered into tolling agreements with the defendant directors to December 2021.

On October 16, 2018, the Company's board of directors received a shareholder demand to investigate and commence legal proceedings against certain members of the Company's board of directors. The demand alleges facts that are substantially similar to the facts alleged in the CAC and the Pacheco complaint and asserts claims that are substantially similar to the claims asserted in the Pacheco complaint. On January 30, 2019, the Company's board of directors received a second shareholder demand from a different shareholder to investigate and commence legal proceedings against certain current and former members of the Company's board of directors based on allegations that are substantially similar to the allegations contained in the first demand letter. These shareholder demands have been referred to a demand review committee of the Company's board of directors. The Company has entered into tolling agreements with the directors named in the demands to December 2021.

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

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

*The following discussion and analysis of our financial condition and results of operations should be read together with our financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q and the audited financial statements and related notes and management's discussion and analysis of financial condition and results of operations for the year ended December 31, 2020 included in our Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 4, 2021. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties and should be read together with the "Risk Factors" section of this Quarterly Report on Form 10-Q for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.*

### Overview

We are a science-driven biopharmaceutical company focused on the discovery and development of novel treatment options for retinal diseases with significant unmet medical needs. We are currently developing both therapeutic product candidates for age-related retinal diseases and gene therapy product candidates for orphan inherited retinal diseases, or IRDs. We believe that both therapeutics and gene therapy serve important roles in drug development and providing potential treatment options for patients suffering from retinal diseases.

Our therapeutics portfolio consists of our clinical stage product candidate Zimura® (avacincaptad pegol), a complement C5 inhibitor, and our preclinical product candidate IC-500, a High temperature requirement A serine peptidase 1 protein, or HtrA1, inhibitor. 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 an orphan inherited condition characterized by progressive damage to the central portion of the retina, or the macula, and other retinal tissue, leading to loss of vision.

We are continuing to recruit and enroll patients in GATHER2, our Phase 3 clinical trial evaluating the safety and efficacy of Zimura for the treatment of GA secondary to AMD, and expect to complete patient enrollment during the third quarter of 2021. We are developing IC-500 for GA secondary to AMD and potentially other age-related retinal diseases.

Our gene therapy portfolio consists of two product candidates in preclinical development (IC-100 and IC-200) 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, or LCA10, 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, or Usher 2A, and *USH2A*-associated non-syndromic autosomal recessive retinitis pigmentosa.

We are developing IC-100 for RHO-adRP and IC-200 for *BEST1*-related IRDs.



**Research and Development Pipeline**

We have summarized the current status of our ongoing research and development programs in the table below.

	Indication	Res	Pre-clin	P1	P2	P3	Status / Milestones
Therapeutics	<b>Zimura:</b> GA secondary to AMD						<ul style="list-style-type: none"> <li>GATHER1 (1<sup>st</sup> Phase 3): Positive 12 &amp; 18-month data reported</li> <li>GATHER2 (2<sup>nd</sup> Phase 3): Target completion of enrollment <b>3Q 2021</b></li> </ul>
	<b>Zimura:</b> Stargardt Disease						<ul style="list-style-type: none"> <li>Expanded enrollment (up to ~25 additional patients) ongoing</li> </ul>
AAV Gene Therapies	<b>IC-500 (anti-HtrA1):</b> GA secondary to AMD						<ul style="list-style-type: none"> <li>Plan to file IND in <b>2H 2022</b></li> </ul>
	<b>IC-200:</b> BEST1-related IRDs						<ul style="list-style-type: none"> <li>Plan to initiate Phase 1/2 in <b>2H 2021</b></li> </ul>
	<b>IC-100:</b> RHO-adRP						<ul style="list-style-type: none"> <li>Evaluating pre-clinical data; regulatory interaction planned</li> </ul>
	<b>miniCEP290:</b> LCA10						<ul style="list-style-type: none"> <li>Lead construct identified; planning development</li> </ul>
	<b>miniABCA4:</b> Stargardt Disease*						<ul style="list-style-type: none"> <li>Additional results expected in <b>2Q 2021</b></li> </ul>
	<b>miniUSH2A:</b> USH2A-related IRDs*						<ul style="list-style-type: none"> <li>Preliminary results expected in <b>2H 2021</b></li> </ul>

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

**Therapeutic Development Programs**

**Zimura**

Zimura, our complement C5 inhibitor, is a chemically-synthesized, pegylated RNA aptamer. Aptamers are short molecules made up of a single stranded nucleic acid sequence or amino acid sequence that binds molecular targets with high selectivity and specificity. The following are brief descriptions of the status of the GATHER1 trial, which we completed in June 2020, and our ongoing clinical trials for Zimura and our manufacturing activities for Zimura.

*GATHER1 (GA secondary to AMD - Completed)*

GATHER1, also known as OPH2003, is an international, randomized, double-masked, sham controlled, multi-center Phase 2/3 clinical trial evaluating the safety and efficacy of Zimura for the treatment of GA secondary to AMD. We enrolled 286 patients in this trial across multiple treatment groups, including various Zimura doses and sham control groups, and patients were treated and followed for 18 months. In October 2019, we announced positive 12-month data from this trial and in June 2020, we completed this trial and announced 18-month data from this trial, which supported the 12-month data. We believe that the GATHER1 trial qualifies as the first of two Phase 3 trials typically required by the FDA for marketing approval of a pharmaceutical product.

*GATHER2 (GA secondary to AMD - Ongoing)*

GATHER2, also known as ISEE2008, is an international, randomized, double-masked, sham controlled, multi-center Phase 3 clinical trial evaluating the safety and efficacy of Zimura for the treatment of GA secondary to AMD. In this trial, we plan to enroll approximately 400 patients, who are randomized to receive either monthly administration of Zimura 2 mg or sham during the first 12 months of the trial, at which time the primary efficacy analysis of the mean rate of change of GA growth over 12 months, as measured by fundus autofluorescence based on readings at three time points: baseline, month 6 and month 12, calculated using the square root transformation of the GA area, which is the same primary efficacy endpoint we used for the GATHER1 trial, will be performed. The design of GATHER 2 is similar to the design of the previously completed GATHER1 trial. If the 12-month results from GATHER2 are positive, we plan to file applications with the FDA and the EMA for marketing approval of Zimura for GA secondary to AMD. At month 12, we plan to re-randomize patients in the Zimura 2 mg arm to receive either monthly or every other month administration of Zimura 2 mg. The final evaluation will take place at month 24.

In June 2020, we dosed the first patient in this trial. We are continuing to recruit and enroll patients and expect to complete patient enrollment during the third quarter of 2021. Meanwhile, we continue to monitor the COVID-19 pandemic closely and may need to slow down or stop patient enrollment in certain geographies depending on the local situation.



### *STAR (STGD1 - Ongoing)*

STAR, also known as OPH2005, is an international, randomized, double-masked, sham controlled, multi-center clinical trial evaluating the safety and efficacy of Zimura for the treatment of STGD1. STAR, similar to GATHER1, 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. If the results are positive and statistically significant, we believe this trial could potentially serve as a clinical trial that can support an application for marketing approval. We initially enrolled 95 patients in the STAR trial. All of these initially enrolled patients had completed their scheduled visits as of September 2020.

In July 2020, we reopened enrollment in this trial in the United States. We plan to enroll approximately 25 additional patients, with the goal of enrolling a total of approximately 120 patients. Similar to GATHER2, we continue to monitor the COVID-19 pandemic closely and may need to slow down or stop patient enrollment in certain geographies depending on the local situation. Newly enrolled patients are randomized on a 1:1 basis to be treated with either Zimura 4 mg or sham for 18 months. We have been and plan to remain masked to the treatment group 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.

### *Zimura Manufacturing*

In early 2017, we completed the small scale manufacture of multiple batches of Zimura drug substance that we are using to support clinical drug supply for the GATHER2 trial and the expanded STAR trial. We have initiated activities in preparation for the scale-up and validation of the manufacturing process for Zimura drug substance with a new manufacturer, with the goal of assessing whether this manufacturer can produce Zimura drug substance at an adequate scale for future potential commercial use. If this manufacturer is successful, we intend for this manufacturer to be our primary supplier of Zimura drug substance. We have also engaged our historical contract manufacturer for Zimura drug substance, Agilent Technologies, Inc., or Agilent, for scale-up and validation activities. Depending on the success of the scale-up activities by the new manufacturer, we may use either this new manufacturer, Agilent or both for future supply of Zimura drug substance. In addition, regardless of which manufacturer we use, we will need to demonstrate that the drug substance produced through the scaled-up process is analytically comparable to the drug substance we are currently using. We are continuing analytical method development and qualification with our contract manufacturers and laboratories.

In 2020, we engaged a contract manufacturer to provide us with additional supply of finished Zimura drug product to support our needs for the GATHER2 trial and the expanded STAR trial. We expect that this contract manufacturer will be able to supply sufficient finished Zimura drug product for these two clinical trials. In addition, we are planning to make a change to the existing vial used for Zimura drug product, which we believe may allow us to support a more efficient fill/finish operation at a commercial scale. We have been in discussions with our historical fill/finish manufacturer, Ajinomoto Bio-Pharma Services, or Ajinomoto, regarding its capacity to supply us with finished Zimura drug product with the new vial for potential commercial use.

We order the polyethylene glycol, or PEG starting material used to make Zimura drug substance from a sole source third-party manufacturer outside the United States. We currently procure the supply on a purchase order basis and are planning to enter into a long-term supply agreement with this manufacturer for the PEG starting material. We are assessing this supplier's capacity to supply the PEG at the scale that we expect we will need for commercial manufacturing.

### **IC-500: HtrA1 Inhibitor**

We are pursuing the preclinical development of IC-500 for the treatment of GA secondary to AMD and potentially other age-related retinal diseases. We have selected IC-500 as the lead compound from our HtrA1 inhibitor program, which includes a number of small molecule compounds that show high affinity and specificity for HtrA1 when tested in vitro.

In early 2021, we completed a review of our IC-500 development program, which we had previously designed to support monthly dosing in our planned first-in-human clinical trial. We believe that we may be able to establish, at an earlier stage of development, a dosing regimen for IC-500 with less frequent dosing than we had previously planned. As a result, we have revised our development plans and timelines for IC-500 with the goal of including both monthly dosing and a less frequent dosing regimen in our first-in-human clinical trial. We have recently initiated our first preclinical tolerability study for IC-500 and are planning additional preclinical studies, including pharmacokinetic and target engagement studies. We are continuing formulation optimization and other manufacturing activities for IC-500. Based on current timelines and subject to successful preclinical development and cGMP manufacturing, we expect to file an investigational New Drug application, or IND, for IC-500 during the second half of 2022.

## Gene Therapy Research and Development Programs

### IC-200: Product Candidate for *BEST1*-Related IRDs

We are pursuing the preclinical development of IC-200, our novel AAV gene therapy product candidate for the treatment of *BEST1*-related IRDs. We and the University of Pennsylvania, or Penn, have conducted a number of preclinical studies of IC-200 and natural history studies of patients with *BEST1*-related IRDs. We are completing a preclinical toxicology study of IC-200 in the naturally occurring canine model of Best disease. In addition, we are working with a gene therapy contract development and manufacturing organization, or CDMO, for preclinical and Phase 1/2 clinical supply of IC-200. We are completing manufacturing and release activities for a cGMP batch produced by our CDMO. Based on current timelines and subject to successful completion of preclinical development, we plan to file an IND and subject to regulatory review, begin patient enrollment in a Phase 1/2 clinical trial for IC-200 in the second half of 2021.

### IC-100: Product Candidate for *RHO*-adRP

We are pursuing the preclinical development of IC-100, our novel AAV gene therapy product candidate for the treatment of *RHO*-adRP. We and Penn have conducted a number of preclinical studies of IC-100 and a natural history study of *RHO*-adRP patients. In addition, we are working with a gene therapy CDMO for preclinical and Phase 1/2 clinical supply of IC-100. We have recently completed the manufacturing and release of a cGMP batch produced by our CDMO.

We have completed two preclinical toxicology studies of IC-100, one of which was a toxicology and efficacy study in the naturally occurring canine model of *RHO*-adRP and the other study was a GLP toxicology study in non-human primates. We tested the same three doses of IC-100 in both studies. In the canine study, we believe the results demonstrated there was efficacy across all three dose groups. We observed, through clinical examination, ocular inflammation in the high dose group in the canines and at varying degrees at different dosing levels in the non-human primates. Because of the different findings across the two species, we are planning to discuss with the FDA the design of our planned first-in-human clinical trial before submitting an IND. We now believe that IC-100 will likely be delayed from entering into a Phase 1/2 clinical trial this year.

### Minigene Programs

AAV vectors are generally limited as a delivery vehicle by the size of their genetic cargo, which is restricted to approximately 4,700 base pairs of genetic code. The use of minigenes seeks to deliver a smaller but still functional form of a larger gene packaged into a standard-size AAV delivery vector. The goal of minigene therapy is to deliver a gene expressing a protein that, although smaller than the naturally occurring protein, is nonetheless functional for purposes of treating the associated disease.

We are funding several sponsored research programs at the University of Massachusetts Medical School, or UMMS, seeking to use a minigene approach to develop new gene therapies for several orphan IRDs. The following is a summary of these minigene programs and their status:

- **miniCEP290 (LCA10):** This program, which we refer to as the miniCEP290 program, is targeting LCA10, which is associated with mutations in the *CEP290* gene. In July 2019, we entered into a license agreement with the University of Massachusetts, or UMass, for exclusive development and commercialization rights to this program. The sponsored research has yielded a number of minigene constructs that show encouraging results when tested in a mouse model. UMMS has conducted additional experiments to optimize constructs, which were delayed during 2020 because of restrictions placed by UMMS on animal research activities as a result of the COVID-19 pandemic. We have recently identified a lead construct from this program and are considering development plans for this program.
- **miniABCA4 (STGD1):** This program, which we refer to as the miniABCA4 program, is targeting STGD1, which is associated with mutations in the *ABCA4* gene. UMMS generated and evaluated several *ABCA4* minigene constructs in both *in vitro* and *in vivo* experiments, which yielded what we believe to be encouraging results. We expect to receive additional results from the miniABCA4 program during the second quarter of 2021.
- **miniUSH2A (USH2A-related IRDs):** This program, which we refer to as the miniUSH2A program, is targeting IRDs associated with mutations in the *USH2A* gene, including Usher 2A and *USH2A*-associated non-syndromic autosomal recessive retinitis pigmentosa. Some of the activities in this program were delayed during 2020 as a result of the closure of UMMS animal research laboratories due to the COVID-19 pandemic. We expect to receive preliminary results from this program during the second half of 2021.

In addition to the license agreement for the miniCEP290 program, UMMS has granted us an option to obtain an exclusive license to any patents or patent applications that result from any of these sponsored research programs.

## **Impact of COVID-19**

Beginning in March 2020, 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 the initiation of patient enrollment in our GATHER2 trial. Although we initiated patient enrollment in June 2020 and our clinical trial sites are continuing to enroll patients, we and our clinical trial sites are doing so cautiously in light of new health and safety practices put into place as a result of the COVID-19 pandemic. We are continuing to monitor the situation closely and may need to slow down or stop patient enrollment in certain geographies depending on the local situation. In addition, we have added sites to this trial because of the ongoing and variable nature of the pandemic and its potential impact on patient recruitment and retention. Health authorities and ethics committees in certain countries have 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. We may face difficulties in recruiting or retaining patients or maintaining scheduled visits to the extent patients are affected by the virus or are fearful of visiting or traveling to our clinical trial sites because of the pandemic. We are aware that a number of patients initially enrolled in the STAR trial missed consecutive visits during the early months of the pandemic. We do not yet know whether the number of missed visits will increase or decrease among the newly enrolled patients in the STAR trial or how many missed visits will occur in the GATHER2 trial, or what the impact of missed visits may be on trial results, especially because we are masked to the treatment of patients during the conduct of the trials. At this time, we do not know whether there will be further impacts on the timing and progress of patient enrollment or on patient retention or maintenance of scheduled visits in any of our ongoing or planned clinical trials as a result of the COVID-19 pandemic.
- Although most of our clinical trial sites have reopened and are continuing to conduct patient visits for our clinical trials, they are doing so with fewer staff and other restrictions and many of them are focusing on more urgent matters rather than clinical trials. We are engaging with our clinical trial sites, with the goal of monitoring the health and well-being of our patients who remain in our trials and maintaining their scheduled visits and treatments. Where possible, we and our clinical investigators have instituted practices such as flexible scheduling of visits for patients and remote monitoring, and we have also provided patient travel services and personal protective equipment to support our sites and patients. During late 2020 to early 2021, a number of our clinical trial sites scaled back their operations because of recent surges in COVID-19 cases or new lockdown measures being imposed. We have been and will continue to monitor the situation closely.
- 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. For example, the closure of animal research laboratories at UMMS for several months during 2020 caused delays to the progress of, and to our timelines for receipt of data from, our collaborative gene therapy sponsored research programs. Additionally, we were unable to perform person-in-plant (PIP) observations on a number of critical manufacturing activities at our CDMO for IC-100 and IC-200, which caused minor delays to our manufacturing timelines for both product candidates. Furthermore, because of the COVID-19 pandemic and restrictions on remote auditing due to privacy and other concerns, we have experienced difficulties and delays in performing audits on most of our clinical trial sites. In addition, a number of our vendors are also servicing other clients who are developing vaccines or medicines for the COVID-19 pandemic and those vendors may prioritize those other customers over us. At this time, we do not know whether there will be further impact on the work of our third-party vendors and collaborators due to the COVID-19 pandemic. We have and will continue to remain in close communication with our vendors.
- Shortages, delays and governmental restrictions arising from the COVID-19 pandemic have disrupted and may continue to disrupt the ability of our contract manufacturers to procure items, such as raw materials, that are essential for the manufacture of our product candidates. For example, during 2020, our contract manufacturer for IC-500 experienced a shortage in obtaining one of the critical raw materials that was sourced from China, which was caused by the shutdown of local suppliers and the slowdown in trade due to the COVID-19 pandemic. This shortage delayed our process development activities for the drug substance for IC-500 by a number of months. In addition, since 2020, there have been shortages of various animals used in research studies, such as several types of non-human primates, which are typically sourced from China, due to the COVID-19 pandemic and disruptions to the global supply chain. Although our development programs have not yet been affected by these shortages, we are continuing to monitor the situation.

- We instituted company-wide remote working starting in March 2020 and expect to continue working remotely for the foreseeable future. We have been relying on remote means of working and communication both internally and externally. We are continuing to monitor and support the health and well-being of our employees and their productivity as remote working continues.

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 for the three months ended March 31, 2021. The progression of the COVID-19 pandemic remains fluid and its impact on our business and operations remains uncertain. 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, including the availability and administration of vaccines, and the economic impact on local, regional, national and international markets. 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.

For further information on actual and potential impacts to us as a result of the COVID-19 pandemic, see the other sections of this Management's Discussion and Analysis of Results of Operations and Financial Position and the Risk Factors contained in this Quarterly Report on Form 10-Q.

### ***Business Development and Financing Activities***

As we continue the development of our product candidates and programs and evaluate our overall strategic priorities, we will continue to pursue selective business development and financing opportunities that advance us toward our strategic goals. We continue to explore potential collaboration and out-licensing opportunities for the future development and potential commercialization of our product candidates. In addition, we plan to continue to evaluate, on a selective and targeted basis, opportunities to potentially obtain rights to additional product candidates and technologies for retinal diseases, including technologies that may complement our existing product candidates and other strategic lifecycle initiatives.

For information about our follow-on public offerings and private placement that we completed in December 2019 and June 2020, please see the Liquidity and Capital Resources section of Management's Discussion and Analysis of Financial Condition and Results of Operations. We expect to continue to pursue capital raising transactions when they are available on terms favorable to us and if the opportunity advances our strategic goals.

### ***Financial Matters***

As of March 31, 2021, we had cash, cash equivalents and available for sale securities of \$180.2 million. We estimate that our year-end 2021 cash, cash equivalents and available for sale securities will range between \$125 million and \$135 million. We also estimate that our cash, cash equivalents and available for sale securities will be sufficient to fund our planned capital expenditure requirements and operating expenses, excluding any potential approval or sales milestones payable to Archemix or any commercialization expenses for Zimura, into 2024. These estimates are based on our current business plan, which includes the continuation of our ongoing clinical development programs for Zimura, the progression of our IC-100 and IC-200 programs into the clinic, and the advancement of our IC-500 development program. These estimates also assume that we will enroll approximately 400 patients in the GATHER2 trial. These estimates do not reflect any additional expenditures related to potentially studying Zimura in other indications, or resulting from the potential in-licensing or acquisition of additional product candidates or technologies, commencement of any new sponsored research programs, or any associated development we may pursue. We have based these estimates on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect.

### ***Financial Operations Overview***

#### ***Revenue***

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

Our ability to become and remain profitable depends on our ability to generate revenues 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.

### **Research and Development Expenses**

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

- external research and development expenses incurred under arrangements with third parties, such as academic research collaborators, contract research organizations, or CROs, CDMOs and other vendors for the production and analysis of drug substance and drug product; and
- employee-related expenses for employees dedicated to research and development activities, including salaries, benefits and share-based compensation expense.

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

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

The following table summarizes our research and development expenses for the three months ended March 31, 2021 and 2020:

	Three Months Ended March 31,	
	2021	2020
	(in thousands)	
Zimura	\$ 10,702	\$ 4,486
IC-500: HtrA1	387	326
IC-100: RHO-adRP	553	2,509
IC-200: BEST1	1,311	2,222
Other gene therapy	10	533
Personnel-related	4,096	2,507
Share-based compensation	1,343	1,153
Other	147	14
	<u>\$ 18,549</u>	<u>\$ 13,750</u>

As we continue our ongoing clinical trials and our ongoing and planned manufacturing activities for Zimura, we expect our research and development expenses for Zimura to increase. We also expect our research and development expenses for IC-500 to increase as we continue preclinical development. We expect our research and development expenses for each of IC-100 and IC-200 to increase as we complete preclinical development and subject to regulatory review, begin clinical development for those product candidates. We expect our research and development expenses for our other collaborative gene therapy sponsored research programs to decrease as the sponsored research for those programs reaches completion. Our research and development expenses may increase if we decide to pursue the development of Zimura in additional indications, if we in-license or acquire any new product candidates, including from our collaborative gene therapy sponsored research programs, or technologies or if we commence any new sponsored research or development programs.

Although the future development of our product candidates is highly uncertain, we expect the development of our product candidates will continue for at least the next several years. At this time, we cannot reasonably estimate the total remaining costs necessary to complete development, to complete process development and manufacturing scale-up and validation activities and to potentially seek marketing approval for any of our product candidates.

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

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

A change in the outcome of any of these variables with respect to the development of our product candidates could mean a significant change in the costs and timing associated with the development of that product candidate. For example, we are conducting the GATHER2 trial, which is a Phase 3 clinical trial evaluating Zimura for GA, with the expectation that data collected from this trial, if positive, together with other available data, will be sufficient to seek marketing approval for this indication in the United States and the European Union. We may subsequently decide to, or be required by regulatory authorities to, enroll additional patients in the GATHER2 trial beyond our current expectations, conduct additional clinical trials for Zimura in GA or conduct additional nonclinical studies of Zimura in order to seek or maintain regulatory approval or qualify for reimbursement approval. As a result of any of the above, we could be required to expend significant additional financial resources and time on the completion of development of Zimura in GA.

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

#### ***General and Administrative Expenses***

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

#### ***Interest Income***

We currently have invested our cash, cash equivalents and available for sale securities in money market funds, U.S Treasury securities, asset-backed securities and investment-grade corporate debt securities, which generate a nominal amount of interest income.

#### ***Critical Accounting Policies and Significant Judgments and Estimates***

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

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

### Accrued Research and Development Expenses

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

We base our expenses related to academic research collaborators, CROs and CDMOs on our estimates of the services received and efforts expended pursuant to quotations and contracts with such vendors that conduct research and development and manufacturing activities on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the applicable research and development or manufacturing expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in us reporting amounts that are too high or too low in any particular period. There have been no material changes in estimates for the periods presented in this Quarterly Report on Form 10-Q.

### Results of Operations

#### Comparison of Three Month Periods Ended March 31, 2021 and 2020

	Three months ended March 31,		Increase (Decrease)
	2021	2020	
	(in thousands)		
<b>Statements of Operations Data:</b>			
Operating expenses:			
Research and development	\$ 18,549	\$ 13,750	\$ 4,799
General and administrative	8,322	4,998	3,324
Total operating expenses	26,871	18,748	8,123
Loss from operations	(26,871)	(18,748)	8,123
Interest income	77	358	(281)
Other income (expense), net	(1)	5	(6)
Loss before income tax benefit	(26,795)	(18,385)	8,410
Income tax benefit	—	3,309	(3,309)
Net loss	<u>\$ (26,795)</u>	<u>\$ (15,076)</u>	<u>\$ 11,719</u>

#### Research and Development Expenses

Our research and development expenses were \$18.5 million for the three months ended March 31, 2021, an increase of \$4.8 million compared to \$13.8 million for the three months ended March 31, 2020. The increase in research and development expenses for the three months ended March 31, 2021 was primarily due to a \$6.2 million increase in costs associated with Zimura, and a \$1.8 million increase in personnel costs, including share-based compensation associated with additional research and development staffing. These increases were partially offset by a \$2.0 million decrease in costs associated with IC-100 and a \$0.9 million decrease in costs associated with IC-200. The increased costs for Zimura were primarily due to the continued start-up and recruitment activities for our GATHER2 trial and increased manufacturing activities. The decreased costs for IC-100 and IC-200 primarily reflect decreased manufacturing and preclinical development activities.



### **General and Administrative Expenses**

Our general and administrative expenses were \$8.3 million for the three months ended March 31, 2021, an increase of \$3.3 million, compared to \$5.0 million for the three months ended March 31, 2020. The increase in general and administrative expenses for the three months ended March 31, 2021 was primarily due to an increase in external costs, including legal and consulting costs associated with litigation, pre-commercialization activities and other administrative costs necessary to support our operations.

### **Interest Income**

Interest income for the three months ended March 31, 2021 was \$0.1 million compared to interest income of \$0.4 million for the three months ended March 31, 2020. The decrease in interest income was primarily due to the decrease in interest rate yields.

### **Income Tax Benefit**

For the three months ended March 31, 2021, the Company recorded no income tax benefit. For the three months ended March 31, 2020, the Company recorded an income tax benefit of \$3.3 million primarily to reflect a settlement of a local tax audit.

### **Liquidity and Capital Resources**

#### **Sources of Liquidity**

Since inception, we have financed our operations primarily through private placements of our common stock and preferred stock, venture debt borrowings, funds received under the Novo Holdings A/S Agreement, our initial public offering, which we closed in September 2013, funds we received under a prior agreement with Novartis Pharma AG related to the licensing and commercialization of Fovista, funds we received in connection with our acquisition of Inception 4, Inc., or Inception 4, in October 2018 and our follow-on public offerings, which we closed in February 2014, December 2019 and June 2020, including the sale of pre-funded warrants in December 2019 and June 2020. We do not have any committed external source of funds.

We currently have an effective universal shelf registration statement on Form S-3, or the Shelf Registration, on file with the SEC registering for sale from time to time up to \$300.0 million of common stock, preferred stock, debt securities, depositary shares, subscription rights, warrants and/or units in one or more registered offerings, of which \$100.0 million may be offered, issued and sold under an “at-the-market” Sales Agreement, or the ATM Agreement, with Cowen and Company, LLC. We have not yet issued and sold any shares of our common stock under the Shelf Registration or the ATM Agreement.

#### **Cash Flows**

As of March 31, 2021, we had cash, cash equivalents and available for sale securities totaling \$180.2 million and no debt. We currently have invested our cash, cash equivalents and available for sale securities in money market funds, U.S. Treasury securities, certain asset-backed securities and certain investment-grade corporate debt securities.

The following table shows a summary of our cash flows for the three months ended March 31, 2021 and 2020:

	<b>Three months ended March 31,</b>	
	<b>2021</b>	<b>2020</b>
	<b>(in thousands)</b>	
Net cash (used in) provided by:		
Operating Activities	\$ (29,457)	\$ (17,526)
Investing Activities	(7,710)	—
Financing Activities	129	179
Net change in cash and cash equivalents	<u>\$ (37,038)</u>	<u>\$ (17,347)</u>

#### **Cash Flows from Operating Activities**

Net cash used in operating activities in the three months ended March 31, 2021 and March 31, 2020 related primarily to net cash used to fund our Zimura clinical trials and manufacturing activities, our preclinical development of IC-100, IC-200 and IC-500, our collaborative gene therapy sponsored research programs and to support our general and administrative operations.



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

#### ***Cash Flows from Investing Activities***

Net cash used in investing activities for the three months ended March 31, 2021 was \$7.7 million, which related to the purchase of marketable securities. We had no net cash used in investing activities for the three months ended March 31, 2020.

#### ***Cash Flows from Financing Activities***

Net cash provided by financing activities was \$0.1 million and \$0.2 million for the three months ended March 31, 2021 and March 31, 2020, respectively, related to stock option exercises and purchases made under our employee stock purchase plan.

#### ***Funding Requirements***

Zimura is in clinical development, our gene therapy product candidates IC-100 and IC-200, and IC-500, the selected product candidate from 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 could incur additional research and development expenses if we modify or further expand the scope of our clinical trials, including if we develop Zimura for additional indications, preclinical development programs or collaborative gene therapy sponsored research programs, or if we in-license or acquire, and undertake development of, additional product candidates and technologies, including any promising product candidates that emerge from our collaborative gene therapy sponsored research programs. We could also incur additional research and development expenses if, for example, we are required by the FDA, the EMA, or regulatory authorities in other jurisdictions, or if we otherwise decide, to perform clinical trials and/or nonclinical or other studies in addition to those we currently expect to conduct. If we experience delays or disruptions to our research and development programs, including delays in patient enrollment or issues with patient retention or patients missing scheduled visits and treatments, if we experience issues with our preclinical development programs, such as unfavorable toxicology or other preclinical data, if we experience issues with the manufacture and supply of product candidates for our development programs, including issues with process development or manufacturing scale-up activities, whether such delays or disruptions are due to the COVID-19 pandemic or other reasons, we could incur additional and unexpected expenses as a result of such delays or disruptions and our business and financial results may be materially impacted. Furthermore, if we successfully develop and expect to 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 UFRE, and Penn with respect to IC-100 and IC-200, UMass with respect to any potential product candidates from our miniCEP290 program, and the former equityholders of Inception 4 with respect to IC-500, 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, 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, STGD1 and potentially other indications;
- 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, IC-200 and IC-500 and pursue our collaborative gene therapy sponsored research programs;
- in-license or acquire the rights to, and pursue the development of, other product candidates or technologies;
- seek marketing approval for any product candidates that successfully complete clinical trials;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, commercial, medical affairs, regulatory, manufacturing, quality control, quality assurance and scientific personnel; and
- expand our general and administrative functions to support our future growth.

As of March 31, 2021, we had cash, cash equivalents and available for sale securities of \$180.2 million. We estimate that our year-end 2021 cash, cash equivalents and available for sale securities will range between \$125 million and \$135 million. We also estimate that our cash, cash equivalents and available for sale securities will be sufficient to fund our planned capital expenditure requirements and operating expenses, excluding any potential approval or sales milestones payable to Archemix or any commercialization expenses for Zimura, into 2024. These estimates are based on our current business plan, which includes the continuation of our ongoing clinical development programs for Zimura, the progression of our IC-100 and IC-200 programs into the clinic, and the advancement of our IC-500 development program. These estimates also assume that we will enroll approximately 400 patients in the GATHER2 trial. These estimates do not reflect any additional expenditures related to potentially studying Zimura in other indications, or resulting from the potential in-licensing or acquisition of additional product candidates or technologies, commencement of any new sponsored research programs, or any associated development we may pursue. We have based these estimates on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect.

We expect we will require substantial, additional funding in order to complete the activities necessary to develop and commercialize one or more of our product candidates. 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 any future Zimura clinical programs and any further development we may undertake to enable us to file a new drug application, or NDA, for Zimura in one or more indications;
- the scope, costs, progress, and results of process development, manufacturing scale-up and validation activities, analytical method development and qualification, and stability studies associated with Zimura and our other product candidates;
- the scope, progress, costs and results of our efforts to develop IC-100, IC-200 and IC-500, including activities to establish manufacturing capabilities and other preclinical development activities 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;
- 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 any of our product candidates;
- the timing and extent of 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;
- 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 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, if we experience 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 decided to enroll

approximately 25 additional patients in our ongoing STAR trial, with the goal of enrolling a total of approximately 120 patients, 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 EMA, or regulatory authorities in other jurisdictions to perform clinical trials or nonclinical 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 are conducting the GATHER2 trial with the expectation that data collected from such trial, if it is positive, together with data from our GATHER1 trial, will be sufficient to support an application for 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 GATHER2 trial beyond our current expectations, conduct additional clinical trials for Zimura in GA or conduct additional nonclinical studies of Zimura in order to seek or maintain marketing approval or qualify for reimbursement approval. In addition, the COVID-19 pandemic may result in disruptions to the progress of the GATHER2 trial or the STAR trial, including slowing patient enrollment or causing enrolled patients to miss their scheduled visits or drop out in greater numbers than we expect, or disruptions 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. 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. For example, we are aware that, in the STAR trial, a number of patients initially enrolled in the trial missed consecutive visits during the early months of the COVID-19 pandemic. We do not know yet whether the number of missed visits will increase or decrease among the newly enrolled patients in the STAR trial or how many missed visits will occur in the GATHER2 trial, and whether and to what extent missed visits may impact the results of any of the trials. 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.

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 and governmental responses to the pandemic have caused 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 \$150 million in net proceeds through our June 2020 public offering and concurrent private placement, 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.

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, declaring dividends or entering into certain investments or transactions. In addition, we have issued, and may in the future issue additional, equity securities as consideration for business development transactions, which may also dilute our existing stockholders' ownership interests.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, products or product candidates or grant licenses on terms that may not be favorable to us. If we choose to pursue a collaboration for any of our

product candidates, 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.

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

### Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of March 31, 2021:

	Payments Due by Period				
	Total	Less than 1 year	1 - 3 years	3 - 5 years	More than 5 years
	(in thousands)				
Sponsored Research (1)	\$ 1,426	\$ 1,426	\$ —	\$ —	\$ —
Purchase Obligations (2)	10,374	10,374	—	—	—
Operating Leases (3)	2,284	912	1,372	—	—
<b>Total (4)</b>	<b>\$ 14,084</b>	<b>\$ 12,712</b>	<b>\$ 1,372</b>	<b>\$ —</b>	<b>\$ —</b>

- (1) This item includes our non-cancelable contractual obligations under our sponsored research agreements.
- (2) This item includes our non-cancelable contractual commitments under certain of our manufacturing and supply agreements.
- (3) This item includes our contractual obligations to make payments in connection with leases for office space.
- (4) This table does not include:
  - any milestone payments which may become payable to third parties under license or acquisition agreements as the timing and likelihood of such payments are not known with certainty;
  - any royalty payments to third parties as the amounts, timing and likelihood of such payments are not known;
  - anticipated expenditures under supply agreements for periods for which we are not yet bound under binding purchase orders; or
  - contracts that are entered into in the ordinary course of business that are not material in the aggregate in any period presented above.

In addition to the amounts set forth in the table above, we may be required, under the agreements under which we acquired rights to Zimura, IC-100, IC-200, IC-500 and our miniCEP290 program, to make milestone payments and/or pay royalties. These payments are described in “Note 9—Commitments and Contingencies” in our unaudited consolidated financial statements appearing elsewhere in this Quarterly Report.

We also have letter agreements with certain employees that require the funding of a specific level of payments if certain events, such as a termination of employment in connection with a change in control or termination of employment by the employee for good reason or by us without cause, occur. For a description of these obligations, see our definitive proxy statement on Schedule 14A for our 2021 annual meeting of stockholders, as filed with the SEC on April 7, 2021.

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

### **Off-Balance Sheet Arrangements**

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

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

We are exposed to market risk related to changes in interest rates. We had cash, cash equivalents and available for sale securities of \$180.2 million as of March 31, 2021, consisting of cash and investments in money market funds, U. S. Treasury securities, corporate debt securities and asset-backed securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because a significant portion of our investments are in short-term securities. Due to the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

We contract with CDMOs, CROs and certain other vendors to perform services outside of the United States. We may be subject to fluctuations in foreign currency rates in connection with certain of these agreements. Transactions denominated in currencies other than the U.S. dollar are recorded based on exchange rates at the time such transactions arise. As of March 31, 2021, substantially all of our total liabilities were denominated in the U.S. dollar.

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

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

Our management, with the participation of our chief executive officer and chief financial officer, evaluated the effectiveness of our disclosure controls and procedures as of March 31, 2021. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Based on the evaluation of our disclosure controls and procedures as of March 31, 2021, our chief executive officer and chief financial officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

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

No changes in our internal control over financial reporting (as defined in Rules 13a-15(d) and 15d-15(d) under the Exchange Act) occurred during the quarter ended March 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

## **PART II**

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

Descriptions of legal proceedings are set forth in “Note 9-Commitments and Contingencies” in the notes to the financial statements filed with this Quarterly Report on Form 10-Q.

## Item 1A. Risk Factors

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

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

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

We are a development-stage company without any approved products. Our growth prospects and the future value of our company are highly dependent on the progress of our research and development programs, including our ongoing and any future clinical trials for Zimura, our preclinical development programs for IC-100, IC-200 and IC-500, and our collaborative gene therapy sponsored research programs. 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 the 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 our research and development programs to generate data to support further development or applications to obtain marketing approval for commercialization, 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 common stock and 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, December 2019 and June 2020. As of March 31, 2021, we had an accumulated deficit of \$591.9 million. Our net loss was \$26.8 million for the three months ended March 31, 2021 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 IC-500, the selected product candidate from 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 could incur additional research and development expenses if we modify or further expand the scope of our clinical trials, including if we develop Zimura for additional indications, preclinical development programs or collaborative gene therapy sponsored research programs, or if we in-license or acquire, and undertake development of, additional product candidates and technologies, including any promising product candidates that emerge from our collaborative gene therapy sponsored research programs. We could also incur additional research and development expenses if, for example, we are required by the FDA, the EMA, or regulatory authorities in other jurisdictions, or if we otherwise decide, to perform clinical trials and/or nonclinical or other studies in addition to those we currently expect to conduct. If we experience delays or disruptions to our research and development programs, including delays in patient enrollment or issues with patient retention or patients missing scheduled visits and treatments, if we experience issues with our preclinical development programs, such as unfavorable toxicology or other preclinical data, if we experience issues with the manufacture and supply of product candidates for our development programs, including issues with process development or manufacturing scale-up activities, whether such delays or disruptions are due to the COVID-19 pandemic or other reasons, we could incur additional and unexpected expenses as a result of such delays or disruptions and our business and financial results may be materially impacted. Furthermore, if we successfully develop and expect to 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, UMass with respect to any potential product candidates from our miniCEP290 program, and the former equityholders of Inception 4 with respect to IC-500, 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, 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, STGD1 and potentially other indications;
- 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, IC-200 and IC-500 and pursue our collaborative gene therapy sponsored research programs;
- in-license or acquire the rights to, and pursue the development of, other product candidates or technologies;
- seek marketing approval for any product candidates that successfully complete clinical trials;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, commercial, medical affairs, regulatory, manufacturing, quality control, quality assurance and scientific personnel; 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 revenues 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 one or more of 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, 2021, we had cash, cash equivalents and available for sale securities of \$180.2 million. We estimate that our year-end 2021 cash, cash equivalents and available for sale securities will range between \$125 million and \$135 million. We also estimate that our cash, cash equivalents and available for sale securities will be sufficient to fund our planned capital expenditure requirements and operating expenses, excluding any potential approval or sales milestones payable to Archemix or any commercialization expenses for Zimura, into 2024. These estimates are based on our current business plan, which includes the continuation of our ongoing clinical development programs for Zimura, the progression of our IC-100 and IC-200 programs into the clinic, and the advancement of our IC-500 development program. These estimates also assume that we will enroll approximately 400 patients in the GATHER2 trial. These estimates do not reflect any additional expenditures related to potentially studying Zimura in other indications, or resulting from the potential in-licensing or acquisition of additional product candidates or technologies, commencement of any new sponsored research programs, or any associated development we may pursue. We have based these estimates on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect.

We expect we will require substantial, additional funding in order to complete the activities necessary to develop and commercialize one or more of our product candidates. 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 any future Zimura clinical programs and any further development we may undertake to enable us to file a new drug application, or NDA, for Zimura in one or more indications;
- the scope, costs, progress, and results of process development, manufacturing scale-up and validation activities, analytical method development and qualification, and stability studies associated with Zimura and our other product candidates;
- the scope, progress, costs and results of our efforts to develop IC-100, IC-200 and IC-500, including activities to establish manufacturing capabilities and other preclinical development activities 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;
- 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 any of our product candidates;
- the timing and extent of 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;
- 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 and governmental responses to the pandemic have caused 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 \$150 million in net proceeds through our June 2020 public offering and concurrent private placement, 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, if we experience 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 decided to enroll approximately 25 additional patients in our ongoing STAR trial, with the goal of enrolling a total of approximately 120 patients, 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 EMA, or regulatory authorities in other jurisdictions to perform clinical trials or nonclinical 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 are conducting the GATHER2 trial with the expectation that data collected from such trial, if it is positive, together with other available data, will be sufficient to support an application for 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 GATHER2 trial beyond our current expectations, conduct additional clinical trials or nonclinical studies of Zimura in order to seek or maintain marketing approval or qualify for reimbursement approval. In addition, the COVID-19 pandemic may result in disruptions to the progress of the GATHER2 trial or the STAR trial, including slowing patient enrollment or causing enrolled patients to miss their scheduled visits or drop out in greater numbers than we expect, or disruptions 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. 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. For example, we are aware that, in the STAR trial, a number of patients initially enrolled in the trial missed consecutive visits during the early months of the COVID-19 pandemic. We do not know yet whether the number of missed visits will increase or decrease among the newly enrolled patients in the STAR trial or how many missed visits will occur in the GATHER2 trial, and whether and to what extent missed visits may impact the results of any of the trials. 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, declaring dividends or entering into certain investments or transactions.

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, 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.

In March 2021, we filed a shelf registration statement on Form S-3, or the Shelf Registration, pursuant to which we may offer and sell shares of common stock, debt securities and other securities for aggregate gross sale proceeds of up to \$300.0 million, of which we may offer and sell up to \$100.0 million from time to time pursuant to an "at-the-market" sales agreement, or the ATM Agreement, we entered into in March 2021 with Cowen and Company, LLC, or Cowen, as agent, subject to the terms and conditions described in the ATM Agreement and SEC rules and regulations. We have not yet issued and sold any shares of common stock under the Shelf Registration or our "at-the-market" offering program. If we make sales under the Shelf Registration or our "at-the-market" offering program, the sales could dilute our stockholders, reduce the trading price of our common stock or impede our ability to raise future capital.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, products or product candidates or grant licenses on terms that may not be favorable to us. If we choose to pursue a collaboration for any of our product candidates, 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, has adversely affected and may continue to negatively affect our business and operations in a number of ways, 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.***

The COVID-19 pandemic, which began in December 2019, has spread worldwide. 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 COVID-19 pandemic 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.

Beginning in March 2020, 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 the initiation of patient enrollment in our GATHER2 trial. Although we initiated patient enrollment in June 2020 and our clinical trial sites are continuing to enroll patients, we and our clinical trial sites are doing so cautiously in light of new health and safety practices put into place as a result of the COVID-19 pandemic. We are continuing to monitor the situation closely and may need to slow down or stop patient enrollment in certain geographies depending on the local situation. In addition, we have added sites to this trial because of the ongoing and variable nature of the pandemic and its potential impact on patient recruitment and retention. Health authorities and ethics committees in certain countries have 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. We may face difficulties in recruiting or retaining patients or maintaining scheduled visits to the extent patients are affected by the virus or are fearful of visiting or traveling to our clinical trial sites because of the pandemic. We are aware that a number of patients initially enrolled in the STAR trial missed consecutive visits during the early months of the pandemic. We do not yet know whether the number of missed visits will increase or decrease among the newly enrolled patients in the STAR trial or how many missed visits will occur in the GATHER2 trial, or what the impact of missed visits may be on trial results, especially because we are masked to the treatment of patients during the conduct of the trials. At this time, we do not know whether there will be further impacts on the timing and progress of patient enrollment or on patient retention or maintenance of scheduled visits in any of our ongoing or planned clinical trials as a result of the COVID-19 pandemic.
- Although most of our clinical trial sites have reopened and are continuing to conduct patient visits for our clinical trials, they are doing so with fewer staff and other restrictions and many of them are focusing on more urgent matters rather than clinical trials. We are engaging with our clinical trial sites, with the goal of monitoring the health and well-being of our patients who remain in our trials and maintaining their scheduled visits and treatments. Where possible, we and our clinical investigators have instituted practices such as flexible scheduling of visits for patients and remote monitoring, and we have also provided patient travel services and personal protective equipment to support our sites and patients. During late 2020 to early 2021, a number of our clinical trial sites scaled back their operations because of recent surges in COVID-19 cases or new lockdown measures being imposed. We have been and will continue to monitor the situation closely.
- 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. For example, the closure of animal research laboratories at UMMS for several months during 2020 caused delays to the progress of, and to our timelines for receipt of data from, our collaborative gene therapy sponsored research programs. Additionally, we were unable to perform person-in-plant (PIP) observations on a number of critical manufacturing activities at our CDMO for IC-100 and IC-200, which caused minor delays to our manufacturing timelines for both product candidates. Furthermore, because of the COVID-19 pandemic and restrictions on remote auditing due to privacy and other concerns, we have experienced difficulties and delays in performing audits on most of our clinical trial sites. In addition, a number of our vendors are also servicing other clients who are developing vaccines or medicines for the COVID-19 pandemic and those vendors may prioritize those other customers over us. At this time, we do not know whether there will be further impact on the work of our third-party vendors and collaborators due to the COVID-19 pandemic. We have and will continue to remain in close communication with our vendors.
- Shortages, delays and governmental restrictions arising from the COVID-19 pandemic have disrupted and may continue to disrupt the ability of our contract manufacturers to procure items, such as raw materials, that are essential for the manufacture of our product candidates. For example, during 2020, our contract manufacturer for IC-500 experienced a shortage in obtaining one of the critical raw materials that was sourced from China, which was caused by the shutdown of local suppliers and the slowdown in trade due to the COVID-19 pandemic. This shortage delayed our process development activities for the drug substance for IC-500 by a number of months. In addition, since 2020, there have been shortages of various animals used in research studies, such as several types of non-human primates, which are typically sourced from China, due to the COVID-19 pandemic and disruptions to the global supply chain. Although our development programs have not yet been affected by these shortages, we are continuing to monitor the situation.

- We instituted company-wide remote working starting in March 2020 and expect to continue working remotely for the foreseeable future. We have been relying on remote means of working and communication both internally and externally. We are continuing to monitor and support the health and well-being of our employees and their productivity as remote working continues.

The progression of the COVID-19 pandemic remains fluid and its impact on our business and operations remains uncertain. Since late 2020, many countries and regions, including many states in the United States, have experienced a surge in the number of new cases, including as a result of several new mutations to the SARS-COV-2 virus, which caused public health authorities to reimpose restrictive measures. In addition, although the FDA has granted emergency use authorization to three vaccines for this disease, there continue to be challenges with distributing vaccines and administering them to the general population, including as a result of newly discovered side effects affecting one of those vaccines, and the long-term safety and efficacy and ability of these vaccines to slow transmission are largely unknown. In addition, many countries, including several countries where we are conducting the GATHER2 and STAR trials, are lagging behind the United States in administering vaccines to their populations and experiencing longer or more extensive surges in COVID-19 cases. As a result, governments may continue to deploy measures to contain the pandemic 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, including the availability and administration of vaccines, and the economic impact on local, regional, national and international markets. 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 COVID-19 pandemic will be effectively contained, nor can we predict the severity and duration of the impact of the pandemic on our financial condition or operations. 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 to our clinical trials or supply chains, 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 obtaining 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. Additional public health crises and natural disasters, such as future epidemics or pandemics or those resulting from the effects of climate change, may arise in the future. 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, including technologies that may complement our existing product candidates and other strategic lifecycle initiatives. 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 our product candidates. 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 the retina and the competition for those assets is intense. The process of

proposing, negotiating and implementing a license or acquisition of a product candidate or technology 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 option 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 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, manufacturing 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 or in-licensing transactions;
- 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, data or 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 approaches, 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. The shareholder derivative action has been stayed while a special litigation committee of our board of directors investigates the allegations contained in the complaint. 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, including in responding to discovery requests, has caused our management and board of directors to divert time and attention to the litigation and could adversely impact our reputation and further 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 Good Laboratory Practices, or GLP, 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 candidate in humans. Prior to initiating clinical trials, we 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 study we are conducting for IC-200 and the preclinical studies we are conducting and planning to conduct for IC-500, may fail at any point or produce unacceptable or inconclusive results 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. For example, we observed different findings across the two different species in which we tested IC-100 in preclinical toxicology studies, which has led us to plan to discuss with the FDA the design of our planned first-in-human clinical trial before submitting an IND. As a result, we now believe that IC-100 will likely be delayed from entering into a Phase 1/2 clinical trial this year.

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 a statistically significant efficacy signal. Additionally, although the 18-month results from our GATHER1 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 while maintaining a favorable safety profile, these results may not be replicated in the GATHER2 trial or any future trials 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, or PEG, used for the manufacture of Zimura, and issues with 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 any BEST1-related IRDs, in either the United States or the European Union, the regulatory pathway for product candidates in those indications, including the selection of efficacy endpoints, 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 or nonclinical studies 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. This risk 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, including the costs of manufacturing activities to support those clinical trials, 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 otherwise change our clinical development plans, 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 continuing to enroll patients in the GATHER2 trial, we may later decide to or be required to slow down or pause patient recruitment due to the continued persistence of the pandemic or as a result of governmental measures instituted in response to the pandemic. Furthermore, our development plans may change based on feedback we may receive from regulatory authorities throughout the development process or for other reasons. 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 marketing approval to the FDA and EMA are based on our review of the 12-month and 18-month data from the GATHER1 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 GATHER1 trial, as we conduct our GATHER2 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 or in any other indication we may choose to pursue.***

We are currently 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 of selective molecular targets, including complement C5, as potential pharmaceutical treatments for GA secondary to AMD, and that the results from our GATHER1 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 nonclinical scientific literature supporting the potential use of complement system inhibitors for the treatment of STGD1, we have not yet completed a clinical trial assessing Zimura for the treatment of STGD1 and do not have any unmasked data regarding the efficacy of Zimura in this indication. As a result, this approach may not prove clinically successful.

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 GATHER1 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 may decide to pursue clinical development of Zimura for other indications, including those we previously studied such as wet AMD and IPCV and other indications such as earlier stages of AMD. Similar to GA and STGD1, Zimura, and the use of C5 inhibition, are unproven in those indications and we may not be successful in our efforts to develop Zimura for those indications.

***We are conducting post-hoc analyses of the results and individual patient level data from the GATHER1 trial, which may yield information that is inconsistent with our conclusions regarding the GATHER1 data. The GATHER2 trial may yield results that are different from the results observed in the GATHER1 trial. An unfavorable result from the GATHER2 trial likely would materially adversely affect our ability to obtain approval for Zimura in GA.***

We are conducting post-hoc analyses of the individual patient level data from the GATHER1 trial. These analyses may yield information that is inconsistent with our conclusions regarding the GATHER1 data, including as a result of previously unknown variables or patient sub-groups that could potentially be driving the results in one or more treatment groups. Although not reported as related to Zimura by investigators, we observed an increase in the number of investigator-reported cases of choroidal neovascularization, or CNV, in the Zimura treatment groups in the GATHER1 trial as compared to the sham control groups. Additionally, we learned from our independent masked reading center that the retinal images of one of the patients in the Zimura 4 mg group showed evidence of CNV in the study eye that was not reported by the investigator. As we continue to evaluate the individual, unmasked patient data from the GATHER1 trial, we may learn of additional cases of non-investigator reported safety issues, which may affect the safety profile of Zimura.

Unlike the GATHER1 trial, the GATHER2 trial includes 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 both our GATHER1 trial and our GATHER2 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 GATHER2 trial consisting of a single monthly administration of Zimura 2 mg, because the 12-month data from the GATHER1

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 GATHER1 trial. Additionally, for our GATHER2 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 GATHER2 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 GATHER2 trial are positive, would in all likelihood provide for monthly administration of Zimura.

We are conducting the GATHER2 trial at many clinical trial sites and in many countries that were not included in the GATHER1 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 trial 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 GATHER1 trial suggested there is an overall dose response relationship in which higher doses of Zimura (for example, the 4 mg and the 2 mg doses) 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, the 1 mg dose). For our GATHER2 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 GATHER1 trial, the protocol of the GATHER2 trial provides that patients who develop CNV in the study eye in the trial may remain in the trial and receive either Lucentis® or Eylea® in accordance with the label for that anti-VEGF agent, and that measurements of these patients' GA will be included in the primary efficacy analysis if their fundus autofluorescence, or FAF, images can be assessed by the masked reading center. The retention of these patients in the GATHER2 trial may introduce additional variability not present in the GATHER1 trial, as we do not have any data regarding the progression of GA in patients with CNV who receive treatment with an anti-VEGF agent. 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, any such occurrence would reduce the number of patients from whom data is available for analyzing the primary endpoint for this trial and the GATHER2 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 secondary to AMD is subject to a number of assumptions, including that we may be able to rely on the results from our GATHER1 and GATHER2 trials as two adequate and well-controlled, Phase 3 trials typically required by the FDA. The FDA, EMA and other regulatory authorities may not accept the design or results of the GATHER1 trial as a Phase 3 clinical trial, or may not agree with our selection of the primary endpoint for the GATHER1 and GATHER2 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 or nonclinical studies to seek or obtain approval for Zimura in GA.***

Based on the results of our GATHER1 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, measured by FAF based on readings at three time points: baseline, month 6 and month 12, calculated using the square root transformation of the GA area, is a primary endpoint of clinical relevance, in the absence of a demonstrated reduction in the loss of vision, and that data from the GATHER1 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, calculated using the square root transformation, 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 GATHER2 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 GATHER1 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 sufficiency or robustness of the data from our clinical trials, including the GATHER1 trial, until such time as we submit an application for marketing approval and receive a response from the applicable authority. If the GATHER1 trial results are not considered robust, or if regulatory authorities do not accept the study designs of GATHER1 or GATHER2, including our selected primary efficacy endpoint, then in order to seek marketing approval we may need to conduct, in addition to the GATHER2 trial, one or more additional, adequate and well-controlled clinical trials that meets the applicable regulatory requirements in order to obtain sufficiently robust data for an acceptable endpoint 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 GATHER1 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 who 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 mixed-effects repeated measures model, or MRM, analysis, where we imputed the values of missing data based on the values of observed data. We plan to use the same MRM analysis in the GATHER2 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 GATHER1 trial, or with the rate at which patients withdrew from the trial. To the extent patients miss critical visits or drop out of the GATHER2 trial, we face a similar risk with GATHER2.

Although we believe that our GATHER1 trial was adequate and 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 to 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 GATHER1 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 safety or efficacy results from the trial.

Based on informal discussions with the FDA, following the GATHER1 trial, 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 GATHER1 and GATHER2 trials in GA, as well as our STAR trial evaluating Zimura for STGD1. We also believe that, if the data from the GATHER2 trial are positive, we would be able to submit our application following the primary efficacy analysis for the GATHER2 study at the 12-month time point, without waiting for the full 24-month data package, which we would collect after submitting for marketing approval and use to supplement our applications for marketing approval while they are pending. We have designed our GATHER2 trial to meet these requirements, which, as we understand them, and if data from the GATHER2 trial are positive, will permit us to seek marketing approval for Zimura in GA in the United States and potentially the European Union. Since receiving the 12-month results from the GATHER1 trial, we have not had an end of phase 2 or other formal meeting with either the FDA or the EMA and we may not do so before receiving results from the GATHER2 trial and submitting our applications for marketing approval. In addition, we have been engaging with various regulatory authorities, including competent national authorities in Europe, during the GATHER2 trial, and expect to continue engaging with regulatory authorities, including with the FDA as part of the fast track program. We may receive feedback that is not consistent with our expectations, including potential disagreements by the EMA and other regulatory authorities with what we 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 GATHER2 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, we may experience a higher than anticipated rate of dropouts and missed visits and treatments in our GATHER2 trial, which could result in our not having adequate safety data for a sufficient number of patients to obtain marketing approval in GA, even if the primary endpoint is met and the results from the GATHER2 trial 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 GATHER1 trial, we may become aware of safety concerns as we analyze individual patient level data in our GATHER1 trial, and they may manifest in our STAR trial, in our GATHER2 trial or in any other subsequent clinical trials we or a potential 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 efficacy data for our GATHER2 trial are similar to those of the GATHER1 trial, any disagreements by the FDA, EMA or other regulatory authorities with GATHER1 will likely affect GATHER2 as well. Our ongoing clinical trials and any future clinical trials or other studies for Zimura that we or a potential collaborator may undertake may yield inconsistent safety or efficacy results with those we have observed to date or otherwise fail to demonstrate sufficient safety or efficacy to justify further development or to ultimately seek or obtain marketing approval. Any negative results from our ongoing or any future clinical trials or other studies 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 or patients with missing visits may reduce the number of patients from whom we can collect and analyze data from STAR. We may not be able to recruit additional patients for this trial in line with our expectations.***

We have no unmasked clinical data regarding the safety and efficacy of Zimura as a treatment for STGD1. As STGD1 is an orphan indication, to our knowledge there is only very limited natural history data currently available regarding the variability of 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 STAR trial, who are generally 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 staffs 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 STAR trial could be underpowered to demonstrate a potential clinical benefit for Zimura in STGD1 with statistical significance.

We have decided to enroll approximately 25 additional patients in this trial, with the goal of enrolling a total of approximately 120 patients. 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. Patient recruitment may take longer or cost more than we would expect.

***The COVID-19 pandemic has affected and may continue to affect the initiation and conduct of our clinical trials, including the recruitment and retention of patients for our GATHER2 and STAR clinical trials. It may have long-lasting effects on the conduct of clinical trials, which can make our ongoing and any future trials more difficult, costly or time consuming.***

Our GATHER1, GATHER2 and STAR trials involve sites located across the United States and in many countries outside the United States. At the start of the COVID-19 pandemic in early 2020, we were in the process of completing patient visits for our GATHER1 trial and those of the initially enrolled patients in the STAR trial, and we were conducting startup activities for the GATHER2 trial. We have made a number of operational changes to our clinical trials as a result of the COVID-19 pandemic, its effects on current and prospective participating patients, and various governmental and other measures in response to the pandemic. As the COVID-19 pandemic evolves, we may make further changes to how we conduct our ongoing and any future clinical trials.

Patient enrollment, missed patient visits and patient retention remain key risks for our clinical trials. Due to the COVID-19 pandemic, we delayed the initiation of patient enrollment for the GATHER2 trial from March 2020 to June 2020. Even though we are continuing to enroll patients in the GATHER2 and STAR trials, we are doing so cautiously in light of the health and safety measures put into place at various clinical trial sites. We may choose to or be required to slow down or stop patient enrollment in certain geographies due to the COVID-19 pandemic and any governmental measures taken in response. Patients, in turn, may be reluctant to enroll in clinical trials or to maintain their scheduled visits and treatments once enrolled due to their reluctance to visit clinical trial sites for fear of potential exposure to COVID-19 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.

For patients who are enrolled in our trials, the COVID-19 pandemic may cause them to miss study visits or drop out in greater numbers than expected, which could affect our ability to complete our trials and obtain data in accordance with our expectations. Compared to the generally elderly patients in our GATHER2 trial, the patients in the STAR trial are generally younger and have work and family commitments, which may cause them to miss more visits or drop out in greater numbers. In addition to the risks posed by increased patient dropouts, if patients miss scheduled visits in greater numbers as a result of the pandemic, especially if a patient misses consecutive visits, it may affect our ability to draw meaningful conclusions from the clinical data. We are aware that a number of patients initially enrolled in the STAR trial missed consecutive visits during the early months of the COVID-19 pandemic. We do not know yet whether the number of missed visits will increase or decrease among the newly enrolled patients in the STAR trial or among the patients in the GATHER2 trial, and whether and to what extent missed visits may impact the results of the trials, especially since we are masked to the data until the conclusion of the trials. The duration of the GATHER2 and STAR trials, at 24 months and 18 months, respectively, plus time for recruiting patients, makes them more likely to be affected by any subsequent waves of the COVID-19 pandemic.

The COVID-19 pandemic has caused many of our clinical trial sites and competent health authorities and ethics committees in certain countries to reduce their staff and operations. This reduction in operations has resulted in delays to the approval of and the site activation process for the GATHER2 trial in certain geographies. As we continue to activate additional clinical trial sites for the GATHER2 trial, the progress of site activation will depend on the local situation in each specific geography. In addition, many sites are focusing on more urgent matters rather than clinical trials, which may delay their ability to recruit patients. During late 2020 to early 2021, a number of our clinical trial sites have been scaling back their operations because of recent surges in COVID-19 cases or new lockdown measures being imposed. Shortages of vaccines, personal protective equipment and other supplies for the prevention of COVID-19 may cause our clinical trial sites to further scale back the number of staff on site and other operations, and may also cause prospective or enrolled patients to avoid clinical trial visits.

In addition to the disruptions to the operations of many clinical trial sites, the COVID-19 pandemic affected our monitoring and audit operations, for example, by requiring remote monitoring, remote source document verification and remote auditing in many instances. Some countries prohibit or limit remote source document verification due to privacy and other concerns. Because of privacy and other concerns with remote auditing, we have experienced difficulties and delays in performing audits on most of our clinical trial sites. Although we do not believe the COVID-19 pandemic has materially affected the robustness of our data verification process for the GATHER1 trial, we may find data verification discrepancies as



we continue to evaluate the individual, unmasked patient level data from the GATHER1 trial. This risk may also affect our data verification processes for the STAR and GATHER2 trials.

***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, our IC-100 product candidate, which we are developing for RHO-adRP, has a mechanism of action that suppresses the expression of endogenous rhodopsin and seeks to replace it with a healthy version of rhodopsin. Patients with autosomal dominant conditions, such as RHO-adRP, have one healthy allele and one mutant disease-causing allele. For patients with RHO-adRP, although the rhodopsin produced by the mutant allele is generally toxic, leading to retinal degeneration, the rhodopsin produced by the healthy allele supports, and may be necessary for, the patient's existing vision. IC-100 may suppress the expression of all endogenous rhodopsin, whether expressed from the healthy or the mutant allele. Treatment with IC-100 may fail to suppress a sufficient amount of the toxic mutant allele or may fail to replace the rhodopsin expressed by the healthy allele to a sufficient degree. Although we believe, based on preclinical experiments in a canine model of RHO-adRP, that IC-100 will restore rhodopsin production to a level sufficient to maintain vision, we will not know this to be the case until we obtain human clinical data regarding IC-100's effect in this patient population.

Moreover, 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 limited number of 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. For example, we observed different findings across the two different species in which we tested IC-100 in preclinical toxicology studies, which has led us to plan to discuss with the FDA the design of our planned first-in-human clinical trial before submitting an IND. These developments have delayed the timelines for IC-100 and we now believe that IC-100 will likely be delayed from entering into a Phase 1/2 clinical trial this year. As we continue to evaluate the results from the preclinical toxicology studies and engage with the FDA, we may decide, or be required to, conduct additional preclinical studies or change our study design for a first-in-human clinical trial for IC-100, which may further delay our timelines for IC-100. Many of the indications for which we are pursuing our gene therapy programs have limited natural history data and limited number of therapies in clinical development, which may make selecting an appropriate endpoint difficult. Furthermore, our gene therapy programs are targeting orphan diseases with relatively small populations, which limits the pool of potential patients for our gene therapy clinical trials. Because gene therapy trials generally require patients who have not previously received any other therapy for the same indication, we will also need to compete for the same group of potential clinical trial patients with our competitors who are also developing therapies for these same indications. 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 IC-500 is also based on a novel mechanism of action that is unproven and poses a number of scientific and other risks.***

IC-500, our selected product candidate from 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 IC-500, and this mechanism of action may not prove safe and effective for these diseases. Although other companies are pursuing HtrA1 inhibition as a strategy for treating retinal diseases, including Genentech in an ongoing Phase 2 clinical trial in GA, to date, there is limited published clinical data regarding the safety and efficacy of HtrA1 inhibition in the target patient population. We are also aware that Genentech recently commenced a clinical trial to assess the long-term safety and tolerability of its monoclonal antibody HtrA1 inhibitor. We made the decision to acquire this program in 2018 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 hypothesis that targeting inhibition of HtrA1 may be a safe and effective method of treating AMD may ultimately be incorrect, which would likely adversely affect the value of IC-500 and its continued development.

To our knowledge, there are no suitable animal models for GA or dry AMD. This absence of a suitable animal model makes designing a proof of concept study to assess the preclinical efficacy of IC-500 difficult. To date, we have not yet generated any preclinical data of IC-500 in animal studies. In addition, we have not had any formal or informal interactions with the FDA or other regulatory authorities regarding our preclinical development plans for IC-500. We do not know whether the FDA or other regulatory authorities will accept any preclinical proof of concept study we may propose, or other aspects of our preclinical development plans for IC-500. The FDA may require us to change our plans or conduct additional studies, which would increase our costs and delay our timelines.



***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. There are a number of known safety risks associated with our product candidates, including gene therapies, and currently unknown safety issues may arise during development.***

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 drugs that initially showed promise in clinical or earlier stage testing have later been found to cause side effects that prevented further development. Safety issues may arise due to reasons unrelated to the study drug, such as issues with the injection procedure or the syringes or needles being used.

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. Although not reported as related to Zimura by investigators, we observed an increase in the number of investigator-reported cases of CNV in the Zimura treatment groups in the GATHER1 trial as compared to the sham control groups. For the GATHER2 trial, because we are asking investigators to perform monthly OCT imaging and to submit cases where patients experience a decrease in visual acuity of five or more ETDRS letters between successive visits to the independent reading center for confirmation by multi-modal imaging, in addition to the cases the investigator suspects to be CNV, we may observe a higher rate of CNV cases in the GATHER2 trial, including, potentially in the Zimura 2 mg treatment group as compared to the sham group. 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 IC-500.

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 GATHER1 trial, we may encounter unknown safety issues as we continue to 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 GATHER2 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 approach may present potentially unknown safety risks when tested in clinical trials that could not have been anticipated based on preclinical studies, including the tolerability studies we are conducting. In addition, if we are successful in formulating IC-500, we intend to administer IC-500 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 procedure in multiple patients with consistency across patients and surgeons. In addition, in order to avoid accelerating damage to a patient'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 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 may encounter manufacturing issues that could cause delays in our development programs or increase costs. We may experience delays in regulatory approval of our product candidates if we or our contract manufacturers do not satisfy applicable 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, IC-500 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 to 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 contract manufacturers, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements. As our contract manufacturer 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, or may need to use an alternative manufacturer. 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 with larger pharmaceutical companies and academic research institutions. 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 conduct our GATHER2 trial and our expanded STAR trial and plan for potential commercialization of Zimura, we and our third-party manufacturers will need to complete several activities to ensure the continued supply of drug product for these trials and adequate preparations to support potential future commercial supply of Zimura. Any delay or failure in completing these activities could cause delays in the development of Zimura or its potential approval or could result in inadequate clinical or commercial product supply.***

In order to obtain and maintain regulatory approval for Zimura, our third-party manufacturers will be required to produce 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 drug substance that we are using to support clinical drug supply for the GATHER2 trial and the expanded STAR trial. Although we believe we have adequate Zimura drug substance for the GATHER2 trial and the expanded STAR trial, this supply may not be sufficient for our needs over the duration of the trials or for any additional trials we may conduct. We have initiated activities in preparation for the scale-up and validation of the manufacturing process for Zimura drug substance with a new manufacturer, with the goal of assessing whether this manufacturer can produce Zimura drug substance at an adequate scale for future potential commercial use. If this manufacturer is successful, we intend for this manufacturer to be our primary supplier of Zimura drug substance. However, this manufacturer may not be successful because of any number of reasons. We have also engaged our historical contract manufacturer for Zimura drug substance, Agilent Technologies, Inc., or Agilent, for scale-up and validation activities. Depending on the success of the scale-up activities by the new manufacturer, we may use either this new manufacturer, Agilent or both for future supply of Zimura drug substance, which may increase our costs and delay our timelines. In addition, regardless of which manufacturer we use, we will need to demonstrate that the drug substance produced through the scaled-up process is analytically comparable to the drug substance we are currently using. If we are unable to demonstrate that the Zimura drug substance produced through the scaled-up process is analytically comparable to the Zimura drug substance we are currently using, including as a result of not having the appropriate assays to demonstrate analytical comparability, our timelines to complete the development of and seek regulatory approval for Zimura would be impacted.

In 2020, we engaged a contract manufacturer to provide us with additional supply of finished Zimura drug product to support our needs for the GATHER2 trial and the expanded STAR trial. We expect that this contract manufacturer will be able to supply sufficient finished Zimura drug product for these two clinical trials. However, we may face issues with releasing batches of finished Zimura drug product from this contract manufacturer, or even if these batches can be successfully released, we may not have sufficient supply for our needs over the duration of these trials or for any additional trials we may conduct. In addition, we are planning to make a change to the existing vial used for Zimura drug product, which we believe may allow us to support a more efficient fill/finish operation at a commercial scale. We have been in discussions with our historical fill/finish manufacturer, Ajinomoto Bio-Pharma Services, or Ajinomoto, regarding its capacity to supply us with finished Zimura drug product with the new vial for potential commercial use. If Ajinomoto is unable to provide us and/or a potential collaborator with Zimura drug product for potential commercial use, we will need to use alternative suppliers, which may increase our costs and delay our timelines.

We order the PEG starting material used to make Zimura drug substance from a sole source third-party manufacturer outside the United States. We currently procure the supply on a purchase order basis and are planning to enter into a long-term supply agreement with this manufacturer for the PEG starting material. However, we may not be able to agree to terms or may need to agree to unfavorable terms in order to secure adequate supply. We are assessing this supplier's capacity to supply the PEG at the scale that we expect we will need for commercial manufacturing. If this supplier is unable to supply us the PEG in line with our expectations, we believe there are a limited number of alternative suppliers for this critical raw material, and if we need to use those suppliers, it could increase our costs and delay our manufacturing plans for Zimura.

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 drug substance manufactured through the scaled up process with the previously manufactured Zimura drug substance, or establish the long-term stability of the Zimura drug product stored in the new vial container. The new manufacturers we have engaged or may engage in the future 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 oligonucleotides such as Zimura. The lack of uniform manufacturing and quality standards among regulatory agencies may delay regulatory approval of Zimura. Furthermore, there are a limited number of contract manufacturers with experience manufacturing oligonucleotides, which may limit our ability to find and use alternative manufacturers.

***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. In 2020, we experienced several delays to our cGMP manufacturing activities for IC-100 and IC-200 because of a number of manufacturing issues at our CDMO. As previously disclosed, due to an issue with one of the starting materials used for our manufacturing process for IC-100, we had to delay our cGMP manufacturing run at our CDMO and reschedule the run for a later date based on the CDMO's availability. There may also be long lead times to manufacture or procure starting materials such as cell banks or plasmids. In particular, plasmids and other starting materials for gene therapy manufacture are usually sole sourced, as there are a limited number of qualified suppliers. The progress of our gene therapy programs is highly dependent on these suppliers providing us or our contract manufacturers with the necessary starting materials that meet our requirements in a timely manner. A failure to procure or a shortage of necessary starting materials likely would delay our manufacturing and development timelines.

A number of factors common to the manufacturing of biologics and drugs could also cause production or quality issues for gene therapies, including raw material or starting material variability in terms of quality, consistency in cell growth, productivity or cell line stability issues, product and process impurities, material shortages of any kind, shipping, distribution, storage and supply chain failures, cell culture 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 have developed our own manufacturing processes, which differ from those originally used by our university collaborators, for example, by using different starting materials and analytical methods. 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 manufacturing systems and done on a smaller scale than what is required for manufacturing for clinical supplies, we may face challenges producing the same product as that produced by the manufacturing processes used by our licensors and other academic collaborators and scaling up the new manufacturing processes as necessary to support supply for clinical trials. 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 and our business may be materially harmed. We have devoted and may need to continue to devote significant time and financial resources to establishing manufacturing processes for IC-100 and IC-200 for IND-enabling preclinical toxicology studies and first-in-human clinical trials for both product candidates. In particular, although our CDMO produced a cGMP batch for IC-100, which has been successfully released, we may encounter issues with completing manufacturing activities for and releasing the cGMP batch of IC-200 produced by that CDMO, which could hamper us from filing an IND and initiating a human clinical trial for IC-200.

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, our contract manufacturers and our contract research organizations 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 or released 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 in the early stages of establishing manufacturing capabilities for IC-500. We may need to conduct additional process development and formulation development activities.***

Before we can commence IND-enabling studies for IC-500, we need to conduct process development and formulation development to determine whether we can identify a viable manufacturing process for and formulate IC-500 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 IC-500, and derive a preparation that includes an adequate amount of drug substance with the necessary inactive ingredients to achieve the desired safety and efficacy profile for intravitreal injection.

We are working with a CDMO to conduct process development, scale up and cGMP manufacturing of the drug substance for IC-500 for preclinical toxicology studies and early-stage clinical trials. We are working with another CDMO to conduct formulation development and optimization activities for the drug product for IC-500. Our contract manufacturers have developed a manufacturing process for IC-500 drug substance and a formulation of this produced drug substance. However, we have only recently begun to test this formulation in preclinical animal studies; the results of these studies may require us to refine or change our manufacturing process or conduct additional formulation development activities. We are in the process of engaging a contract manufacturer to manufacture finished drug product for clinical supply. Manufacturing, including process development, formulation development and drug product manufacturing, can be costly and time-consuming and our anticipated timelines for the development of IC-500 may be delayed. If we are unable to successfully manufacture and formulate IC-500 in line with our expectations, we may switch to a backup HtrA1 inhibitor or cease developing our HtrA1 inhibitor program altogether.

***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.

Our business strategy includes a focus on developing transformative therapies for retinal diseases, including GA secondary to age-related macular degeneration and a number of orphan inherited retinal diseases. There are multiple companies pursuing the development of therapeutics targeting the complement pathway and 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 therapies than we do. Competition in this field is intense and especially 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.

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 enrolling patients 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, such as may be the case for the GATHER2 trial, for which a number of other companies have active clinical trials.

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:*

- We are aware that LumiThera, Inc. has a medical device using its LT-300 light delivery system, which is approved in the European Union for the treatment of dry AMD. In addition, 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 Alexion Pharmaceuticals, Inc., Annexon Inc., Apellis Pharmaceuticals, Inc., or Apellis, Applied Genetic Technologies Corporation, or AGTC, Biogen Inc., Gemini Therapeutics, Inc., Gyroscope Therapeutics, IONIS Pharmaceuticals, Inc. (in collaboration with Roche AG), Janssen Pharmaceuticals Inc. (which acquired its program through the acquisition of Hemera Biosciences, LLC), MorphoSys AG, NGM Biopharmaceuticals Inc. and Novartis AG each have complement inhibitors in development for GA or dry AMD, including, in the cases of Gemini Therapeutics, Gyroscope Therapeutics and Janssen Pharmaceuticals, complement inhibitor gene therapies and AGTC and Gemini Therapeutics each has a research program on complement factor H gene therapy. We believe that the most advanced of these programs is Apellis's pegylated, synthetic peptide targeting complement protein C3, for which Apellis is conducting two Phase 3 clinical trials, and based on the most recent public information available, Apellis expects to announce top-line data from those trials in the third quarter of 2021. If Apellis's Phase 3 clinical trials for its C3 complement inhibitor product candidate are successful, it is likely that Apellis would obtain marketing approval for its product candidate in advance of when we could reasonably expect to obtain marketing approval for Zimura in GA or IC-500 in GA, if at all. Moreover, we are aware that several other companies, including Allergan Inc., Allegro Ophthalmics, LLC, Alkeus Pharmaceuticals Inc., Astellas Pharma Inc., Boehringer Ingelheim, EyePoint Pharmaceuticals, Inc., Lineage Cell Therapeutics, Inc., Roche AG and Stealth BioTherapeutics Corp., are pursuing development programs for the treatment GA or dry AMD using different mechanisms of action outside of the complement system, including Genentech, Inc. (an affiliate of Roche AG) and Gemini Therapeutics, which are pursuing HtrA1 inhibition as a mechanism of action. We believe that the most advanced HtrA1 inhibitor program in development is Genentech's monoclonal antibody HtrA1 inhibitor, which is currently being studied in a Phase 2 clinical trial.

*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 AGTC, Alkeus Pharmaceuticals, Inc., Beam Therapeutics Inc., Generation Bio Co., Kubota Vision Inc. (formerly Acucela), Lin BioScience, Inc., Nightstar Therapeutics plc (prior to its acquisition by Biogen), or Nightstar, ProQR Therapeutics N.V., or ProQR, and Spark Therapeutics each have research or development programs in Stargardt disease. Three of these programs, Alkeus, Kubota and Lin BioScience, are exploring the use of oral therapeutics, while AGTC, Nightstar and Spark are each using a gene therapy approach, Beam is using a base editing approach, and ProQR is using an RNA based approach. Kubota's product candidate, to which the FDA and the EMA granted orphan drug designation in August 2020, is in Phase 3 development while Alkeus's product candidate is in Phase 2 development. In addition, several academic organizations have early stage programs in Stargardt disease.



*Competitive considerations for RHO-adRP:*

- We are aware that ProQR is developing an RNA-based therapeutic for RHO-adRP, for which it is currently conducting a Phase 1/2 clinical trial. Ocugen, Inc. is developing a gene therapy for RHO-adRP, for which the FDA granted orphan drug designation in July 2020. In addition, prior to its acquisition by Biogen, Nightstar had a preclinical AAV gene therapy program in RHO-adRP. 4D Molecular Therapeutics is developing an intravitreal gene therapy for RHO-adRP. Editas Medicine, Inc. is exploring a potential gene editing program in this disease. We are also aware that multiple academic institutions have early stage gene therapy development programs in RHO-adRP.

*Competitive considerations for BEST1-related IRDs:*

- We are aware that, prior to its acquisition by Biogen, Nightstar 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. has a gene editing program for LCA10, for which a Phase 1/2 clinical trial is ongoing, ProQR is developing an RNA-based therapeutic for LCA10 that is currently in Phase 2/3 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 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 is approved, the territories in which the product may be marketed and the commercial potential for such product candidate. We are developing Zimura and IC-500 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, and the likely degree of acceptance of our product candidate by the relevant physicians in various markets.

There are risks involved with establishing our own sales, marketing and distribution capabilities. 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.

There are also risks involved with having third parties perform sales, marketing and distribution services on our behalf. 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 or are unable to 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 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 other stages 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;
- for treatment regimens calling for multiple intravitreal injections on the same day, restrictions in the label imposing a waiting period in between intravitreal 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 treatments such as gene therapy; and
- whether competing products or other alternatives are more convenient or easier to administer, including 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, 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 acceptable 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 GATHER1 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 or sub-studies, 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 STAR 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, market response to anti-VEGF agents currently approved for treatment of wet AMD and to Spark Therapeutics's Luxturna® and Novartis AG's Zolgensma®, third-party research reports and other surveys. The potential market opportunity for our product candidates may also differ across geographies. While we believe that our internal assumptions are reasonable, 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 GA and certain IRDs, likely will diminish the therapeutic benefit conferred by a new drug product due to irreversible cell death. For example, certain GA patients may have experienced the loss of certain portions of retinal tissue that disproportionately affected their functional vision, and these patients may not value a treatment that can only slow the growth of additional GA lesions without providing a treatment to their loss of functional vision. 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 a relative benefit in functional vision 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 three 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 new Biden Administration, the U.S. Congress and many states. For example, the previous 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. In September 2020, the Trump Administration issued an executive order directing the Secretary of the Department of Health and Human Services, or HHS, to propose rulemaking that would limit the prices paid by Medicare for certain drugs and biologics to the "most favored nation" price. If this kind of rule were to be adopted, 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. We expect the Biden Administration to pursue additional rulemaking aimed at limiting drug prices. 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 costs. 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 many members of the U.S. Congress expressed an interest in pursuing. In September 2020, HHS issued 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 financial condition, or our ability to raise capital needed to commercialize products.

For a further discussion of health care reform and other political factors affecting drug prices, see the risk factor herein entitled "*Current and future legislative efforts may limit the prices for our products, if and when they are licensed for marketing, which could materially impact our ability to generate revenues.*"

***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 and the lawfulness of using 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;
- withdrawal of clinical trial participants;
- injury to our reputation and significant negative media attention;

- 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, including to support potential commercialization. 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 have historically relied on, and purchased on a purchase order basis from, a single third-party manufacturer, Agilent, to provide Zimura drug substance. We have engaged a new manufacturer to conduct scale up and validation activities for Zimura drug substance, and if this manufacturer is successful, we intend for this manufacturer to be our primary supplier for Zimura drug substance. However, we do not currently have any contractual commitments with the new manufacturer or Agilent for the long-term clinical or commercial supply of Zimura drug substance. We may ultimately need to rely on the new manufacturer, Agilent or both or other manufacturers for long-term supply of Zimura drug substance. We have also historically relied on a single third-party manufacturer, Ajinomoto, for Zimura drug product. We have engaged a second fill/finish service provider for additional supply of Zimura drug product for our expected needs for the GATHER2 and STAR trials. We plan to rely on Ajinomoto for long-term supply of Zimura drug product using the new vial we have selected. However, we may ultimately need to rely on other manufacturers for long-term supply of Zimura drug product. We purchase the PEG starting material on a purchase order basis from a single third-party supplier. We are in discussions with this supplier for a long-term supply agreement for the PEG starting material. For these and any other manufacturers with which we do not have any contractual commitments for supply, the pricing and other terms for supply may vary, even substantially, over time and could adversely affect our financial results and operations.

We work with a gene therapy CDMO for preclinical and Phase 1/2 clinical supply of IC-100 and IC-200. For IC-500, we work with a CDMO to conduct process development, scale-up and cGMP manufacture of the drug substance for preclinical toxicology studies and early-stage clinical trials and a different CDMO to conduct formulation development activities. We expect to engage a different CDMO to conduct cGMP manufacture of the IC-500 drug product for early-stage 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. We may not have adequate or timely visibility over issues at our third-party manufacturers, and may not become aware of any such issues until the effect on our programs, if any, has already materialized.

Agilent 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. Agilent informed us that as a result of competing demands from other customers, its ability to support our future manufacturing activities for Zimura is limited. As a result, we have engaged a new contract manufacturer, which we intend to become our primary supplier of Zimura drug substance if the scale up efforts at this new manufacturer are successful, 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.

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 and audits. These changes have affected how we work with our manufacturers and have resulted in minor delays to the progress of our manufacturing activities. For example, we were unable to perform person-in-plant (PIP) observations on a number of critical manufacturing activities at our CDMO for IC-100 and IC-200, which caused minor delays to our manufacturing timelines for both product candidates. Additionally, shortages and governmental restrictions arising from the COVID-19 pandemic have disrupted and may continue to disrupt the ability of our contract manufacturers to procure items, such raw materials, that are essential for the manufacture of our product candidates. For example, in 2020, the COVID-19 pandemic and governmental measures in response caused a delay to the process development activities at our drug substance manufacturer for IC-500 as a result of difficulty in procuring one of the critical starting materials used in the manufacture of IC-500 from China. The COVID-19 pandemic may cause additional disruptions to the supply of starting materials for our product candidates.

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. We source the PEG starting material from a supplier outside the United States. Our supplier relationships could be interrupted due to international supply disruptions, including those caused by geopolitical and other issues. For example, trade disputes, trade negotiations or the imposition of tariffs between the United States and its trading partners could cause delays or disruptions in our supply of starting materials for our product candidates.

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

- our product candidates may compete with other product candidates and products for access to a limited number of suitable manufacturing facilities that operate under cGMP conditions;
- reliance on the third party for regulatory compliance, quality assurance and quality control;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how, or the proprietary information of third parties that we are responsible for protecting; and
- the possible termination or non renewal 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 delayed some of 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, analytical 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 models for two of the diseases we are aiming to treat: RHO-adRP and *BEST1*-related retinal diseases. Our preclinical development plans for IC-100 and IC-200 have included conducting certain preclinical studies using the associated canine disease model. In 2020, we experienced some delays in the breeding of the canines for our IND-enabling study for IC-200, which delayed the start of that study for several months. If we need to conduct additional preclinical studies using any of the canine disease models, and these canines are not available to us for any reason, our development of IC-100 or IC-200 could potentially be further 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. During 2020, Penn 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 limited their ability to analyze some of the data generated during our preclinical studies. As a result, our receipt of data and reports from some of those studies was delayed. In addition, we curtailed some of the analysis we had originally planned for one of the preclinical studies for our IC-200 program. The University of Florida, or UF, also limited staff on site in their laboratories and vector production facilities, which delayed our obtaining certain reagents and other materials used for our gene therapy programs. In addition, UMMS suspended researcher access to their laboratories and the conduct of certain animal studies, which delayed our timelines for our miniCEP290 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, including personal protective equipment for site staff, or animals that are used for preclinical studies. For example, there have been shortages of various animals used in research studies, such as several types of monkeys, which are typically sourced from China, due to the COVID-19 pandemic and disruptions to the global supply chain. Although our development programs have not yet been affected by these shortages, we are continuing to monitor the situation. 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, analytical 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. The COVID-19 pandemic has prevented us from performing audits on our vendors and clinical trial sites that we otherwise would have performed, which decreases the level of oversight we have over those vendors and clinical trial sites and increases the risk of non-compliance. 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. For a number of our analytical development and testing providers, our



CDMOs subcontract and manage that work on our behalf and we have less visibility into or control over their activities. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our preclinical studies, analytical testing 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. Our product candidates are required to be stored and shipped at certain temperatures and a deviation from those requirements may result in delays or additional costs. In addition, a number of these vendors are also servicing other clients who are developing vaccines or medicines for the COVID-19 pandemic and those vendors may prioritize those other customers over us. 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. If we exercise our option rights for a program that is attractive to us, we may not be successful at in-licensing rights to the inventions or may need to agree to unfavorable terms.

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 and the hiring of additional qualified personnel. In addition, the development or 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. A number of countries require sponsors to perform a clinical trial in the local jurisdiction or with patients similar to the demographics of the local population as a condition to approving the drug. 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.

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 and other data we have generated for the product candidate, 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, any patent or other forms of exclusivity for such product candidate and 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 business combinations among pharmaceutical and biotechnology companies over the past decade that have resulted in a reduced number of potential future collaborators and this trend is likely to continue.

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 in line with our expectations.

***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 enter into any arrangements with third parties, 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 de-emphasize 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;
- we may be obligated to supply the collaborator with drug substance or drug product in an amount sufficient for its needs, or may be dependent on the supply of certain materials or products by the collaborator;
- disagreements or disputes with collaborators, including disagreements or disputes over proprietary rights, contract interpretation or the preferred course of development or commercialization, 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 expensive, and be uncertain in outcome;

- 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 agree to other conditions that are not attractive to us; and
- collaborations may be terminated at 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. For IC-100, IC-200 and our miniCEP290 program, we are party to agreements with academic institutions, and under those agreements, we must meet certain milestones by certain timelines and if we fail to do so, we may need to expend significant amounts of money to extend those timelines or otherwise be in breach of those agreements. 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 IC-500, also imposes specified diligence and milestone payment obligations on us. We may enter into acquisition or licensing agreements in the future that could 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 and educational 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 on 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, IC-500 and our miniCEP290 program 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, patent laws in Europe and some other jurisdictions generally make the issuance and enforcement of patents that cover methods of treatment of the human body difficult in those jurisdictions. 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 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 not issue as patents. Even if they are issued as patents, any of the claims covering IC-200 may be declared unpatentable or invalid, or the patents may be declared unenforceable. An inability to secure patent coverage for IC-200 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 the portion of the 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 in-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 or protect 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, patent laws in Europe and some other jurisdictions restrict 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, term, validity, 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. In addition, the issuance of any patents will depend on the existence of any prior art that comes to the patent examiner's attention during prosecution, sometimes through the actions of third parties, and whether our claimed invention meets the statutory criteria for being granted a patent in light of the prior art. 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, revised United States patent law in part by changing the standard for patent approval from a "first to invent" standard, which had existed before March 2013, to a "first to file" standard and developing a post-grant review system. 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 and we may not be able to obtain injunctive relief. 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 our collaborators, including our contract manufacturers and any commercial 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 collaborators 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 collaborators 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, use or sale. 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 manufacture or commercialization thereof, does not and will not infringe or otherwise violate any third party's intellectual property.

If we or any of our collaborators 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, manufacturing and marketing our product candidates or products or to continue using a trademark. However, we or our collaborators 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 collaborators and could require us or them to make substantial licensing and royalty payments. We or our collaborators could be forced, including by court order, to cease using or 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 collaborators from making or 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 collaborators 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 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 some of the 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 IC-500 and the other 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 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 IC-500 and our other HtrA1 inhibitors 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 become aware of such breach or may not be able to obtain adequate remedies. 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 our information technology systems and any failure, inadequacy, interruption or security lapse of those 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 business, we collect, process and maintain personal and other sensitive data on our information technology networks. These data include our intellectual property and other proprietary or confidential information relating to our business as well as proprietary or confidential information of third parties including business collaborators. These data also



include personal information relating to our clinical trial participants, employees and contractors, clinical investigators and other study staff and healthcare professionals. 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 an incident response plan and other standard operating procedures for responding to any cyber-security incidents, mandatory routine 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 information technology systems 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 cyber and ransomware 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. In particular, there have been increasing number of cyber threats and attempts by foreign hackers targeted towards U.S. pharmaceutical and biotechnology companies and vendors they work with.

As a result of the COVID-19 pandemic, we have switched to remote working since March 2020 and as a result, have increasingly relied upon teleconferencing and cloud-based means of communication and data storage. 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.

Cyber-attacks have become more prevalent and much harder to detect and defend against. Our networks and storage applications may be subject to unauthorized access by hackers or breached due to human error, malfeasance or other system disruptions. We may not anticipate or immediately detect such incidents and the damage caused by such incidents. System failures, data breaches and any unauthorized access, use or disclosure of our information or data could compromise our intellectual property and expose sensitive business information; lead to unauthorized exposure of personal information of our clinical trial participants, our employees or contractors, our clinical investigators or other study staff, or others we work with; and/or result in disruptions to our research and development activities and business operations, including potential product development, regulatory approval and commercialization delays.

In addition, cyber-attacks and the measures we implement to prevent, detect, and respond to them could cause us to incur significant remediation costs, including costs to recover or reproduce any compromised data, expose us to contractual damages and/or regulatory and other liability, require us to make certain breach notifications, and divert the attention of our management and key information technology resources. Any loss of preclinical data or clinical trial data could result in delays to our product development, marketing approval and commercialization efforts. We may not have adequate insurance coverage to provide compensation for any losses associated with such events and cybersecurity insurance is becoming more expensive. Any breach of security could harm our reputation and deter patients, clinical investigators, or other healthcare professionals and business collaborators from participating in our clinical trials or otherwise working with us.

***We also rely significantly upon the information technology systems of our third-party service providers and any failure, inadequacy, interruption or security lapse of those systems could harm our ability to operate our business effectively. We have limited control and oversight over the information security systems and practices of third parties.***

In the ordinary course of business, we rely on third parties, including clinical trial sites, CROs, CDMOs and other service providers, to collect, process and maintain personal and other sensitive data on their respective networks for our research and development activities and other business operations. These data include our intellectual property and other proprietary or confidential information relating to our business, as well as personal information relating to our clinical trial participants, employees and contractors, and clinical investigators and other study staff. The maintenance of our data by third parties does not absolve us of our responsibility for the security and integrity of this data.

We have limited control and oversight over the information security systems and practices of third parties. Those systems and practices vary widely in sophistication and robustness. We have limited personnel and resources to oversee the information security systems of third parties with whom we work.

Like our information security systems, those of our third-party service providers are vulnerable to compromise, damage, loss or exfiltration from cyber-attacks, computer viruses, unauthorized access and other causes. Our third-party service providers may not anticipate or immediately detect such incidents and the damage caused by such incidents or notify us in a timely or complete manner. System failures, data breaches and any unauthorized access, use or disclosure of our information or data maintained by our third-party service providers could lead to similar consequences for us as similar events involving our information technology systems, including compromise of our intellectual property or other sensitive personal or business information, disruptions and delays to our research and development activities and other operations, contractual and regulatory liability, data breach notifications, expenditure of significant costs and resources for remediation and harm to our reputation.

In September 2020, one of our vendors for the GATHER2 trial suffered a ransomware attack on several of its servers. While this vendor investigated and worked to mitigate the effects of the incident, we deployed a backup process for the work this vendor was performing for us. Although we do not believe this incident had a material impact on the GATHER2 trial or otherwise on our business or operations, similar kinds of incidents may occur in the future with this or our other vendors.

***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 in line with our expectations, 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 personal information is rapidly evolving worldwide 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 and their rights, conducting data protection impact assessments before starting certain 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, some of which are currently in flux, 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 implementing the GDPR that differ from one another. The GDPR compliance framework is evolving as data protection authorities enforce applicable requirements and as European courts interpret the GDPR. 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. 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 being considered, and in certain cases enacted, 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, and its replacement, the California Privacy Rights Act, which will become effective on January 1, 2023, are creating similar risks and obligations as those created by the 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). The New York SHIELD Act, which became fully effective in March 2020, imposes certain data security and data breach notification requirements on organizations that collect personal information of New York residents. Many other states are considering similar legislation. A broad range of legislative measures are being 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 on our behalf. 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, have resulted in certain changes to our business practices, such as additional consideration given to the GDPR and other relevant data protection laws in setting up clinical trial agreements and informed consent forms for our GATHER2 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 applicable 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 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 and in retaining key employees and consultants.***

We are a development-stage company with a total of 65 full-time employees as of April 30, 2021. These employees support key areas of our business and operations, including clinical operations, regulatory affairs, drug safety, data management, medical affairs, scientific research, process and analytical development, drug substance and drug product manufacturing, quality control, materials and supply chain management, and quality assurance, as well as all of our general and administrative functions and public company infrastructure.

We remain highly dependent on Glenn P. Sblendorio, our chief executive officer, and Dr. Pravin U. Dugel, our 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. As we conduct our GATHER2 trial and the expanded STAR trial, prepare for the future development and potential commercialization of Zimura, and continue the development of IC-500 and our gene therapy programs, we have been and expect we will need to continue hiring additional clinical operations, quality assurance, manufacturing, analytical, medical, regulatory and other personnel from this limited pool. We also experience competition for the hiring of scientific, technical and clinical personnel from universities and research institutions. We also have no dedicated commercialization personnel and will need to hire these personnel as we prepare for the potential commercialization of Zimura.

In addition to our employees, we rely on consultants and advisors, including scientific, technical and clinical advisors, to assist us in formulating our research and development, manufacturing, commercialization and lifecycle management 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 for the foreseeable future. Our ability to continue to work remotely and when the conditions are appropriate, transition effectively to working in our offices, may affect our operations and the success of our company going forward.***

In 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 for the foreseeable 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 if and when to transition back to working in our offices. We expect the transition to working in our offices, if any, to occur in stages, which will depend on, among other factors, the local COVID-19 and public safety situation and the degree to which our employees have received vaccines. If and 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 subsequent waves of the COVID-19 pandemic. If any of them contracts COVID-19 as a result of or while conducting services for us, we may be subject to workers compensation or other claims. 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 future material weaknesses or combination of deficiencies could materially and adversely affect our ability to provide timely and accurate financial information and investors' confidence in our internal controls and our company, which could cause our stock price to decline.

#### **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, recordkeeping, labeling, storage, 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's 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 nonclinical, 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 nonclinical 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 nonclinical 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 sold 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. If our third-party commercial partners fail to obtain marketing approval in certain jurisdictions, it may diminish the value of our product candidate to them and cause them to terminate their relationship with us.

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 and European Union rules and regulations ceased to apply to the UK starting on January 1, 2021. In December 2020, the UK government and the European Union agreed on a long-term trade agreement to govern economic relations going forward. 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. We are continuing to analyze how Brexit and the recently concluded trade agreement will affect the future regulatory regime for pharmaceutical products in the United Kingdom. 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 or for other reasons.***

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 or for other reasons.

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 help 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 or similar 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 and that there exists no satisfactory



method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Community or, if such method exists, that the medicinal product will be of significant benefit to those affected by that condition.

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, as the case may be, during that marketing exclusivity period from approving another marketing application for a product that constitutes the same or similar 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 may 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. In the European Union, the exclusivity period can be extended by two years following the completion of an agreed pediatric investigation plan. 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, or a competing sponsor may be allowed on the market, if any regulatory agency determines that the request for designation was materially defective or if the sponsor having orphan drug exclusivity 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 a competing sponsor's drug could nevertheless be approved for the same condition if certain requirements are met. 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 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, tracking of 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 possible 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.

Non-compliance with European Union requirements regarding safety monitoring or pharmacovigilance, and with any applicable requirements related to the development of products for the pediatric population, can also result in significant 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 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 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 \$11,665 and a maximum of \$23,331 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 in connection with the delivery of or payment for benefits, items or services involving a healthcare benefit program;
- 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, and providing notifications of the breach of such information, by covered entities and certain business partners;
- 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 HIPAA and each other in significant ways, 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 Zimura advances in clinical development and toward potential commercialization, 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 are doing business or 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, and as a result, our relationships with those healthcare providers or third parties may be adversely affected and our business and reputation may suffer.

***Current and future legislation may increase the difficulty and costs for us and any future collaborators to obtain reimbursement for any of our product candidates that may receive marketing approval and our ability to generate revenue will be materially impaired.***

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we 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 collaborators, may receive for any approved products. If reimbursement of our products is unavailable or limited in scope, our business could be materially harmed.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA. Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the “individual mandate.” The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseparable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court heard this case on November 10, 2020 and a ruling by the Court is expected sometime this year. Pending resolution of the litigation, all of the provisions in the ACA but the individual mandate to buy health insurance remain in effect. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing 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. On January 28, 2021, however, President Biden issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans’ access to health care, and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

***Current and future legislative efforts may limit the prices for our products, if and when they are licensed for marketing, which could materially impact our ability to generate revenues.***

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of pharmaceutical products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including rebate programs, price controls, restrictions on reimbursement and requirements for substitution of generic products. Efforts to control drug pricing have garnered bipartisan support in U.S. Congress. To that end, the Trump Administration published final rules that 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. Earlier, the FDA had 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). Further, President Trump issued five executive orders intended to lower the costs of prescription drug products. Several of these orders are reflected in recently promulgated regulations, and one of these regulations is currently subject to a nationwide preliminary injunction.

The Biden Administration has frozen certain of the previous administration’s measures to reform drug prices, pending further review. It remains to be seen how the Biden Administration will address this issue, but, under Medicare Part D, the new administration may seek to establish a ceiling for the launch prices of all branded, biologic, and certain generic drugs by referencing the average price of these drugs in other developed countries. At the same time, the administration may seek to limit Medicare Part D and public option drug prices through a tax penalty on manufacturers for increases in the cost of drugs and biologics above the general inflation rate. The American Rescue

Plan Act of 2021, a comprehensive COVID-19 relief law recently enacted under the Biden administration, includes a number of healthcare-related provisions, such as support to rural health care providers, increased tax subsidies for health insurance purchased through insurance exchange marketplaces, financial incentives to states to expand Medicaid programs and elimination of the Medicaid drug rebate cap effective in 2024.

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, 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. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Finally, outside the United States, in some nations, including those of the EU, the pricing of prescription pharmaceuticals is subject to governmental control and access. 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 or our collaborators may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If pricing for our products, if approved and licensed, is set at unsatisfactory levels, our business could be materially harmed.

***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 rely is subject to the political process, which is fluid and unpredictable. For example, over the past decade, 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. We may face impediments to scheduling or conducting regulatory meetings, inspections 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.

***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 have relationships with certain officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations, including a number of public hospitals that are our clinical trial sites. 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

or governmental programs, 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 or our contractors' 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. We expect the new Biden Administration to pass additional such laws and regulations.

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 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, including as a result of short selling by institutional and retail investors. 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. For example, we expect that Apellis will announce top-line data from its Phase 3 program for GA during the third quarter of this year, and that those results will affect the price of our common stock;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- the level of expenses related to any of our product candidates or development programs;
- variations in our financial results or those of companies that are perceived to be similar to us;
- the recruitment or departure of key personnel;
- 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;
- relevant scientific and medical developments;
- 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, social, 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 "*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, and cause additional volatility in the price of our common stock.

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

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. For example, we issued 8,649,453 shares of our common stock to funds affiliated with Vivo Capital, LLC and Samsara BioCapital, LP in a private placement in June 2020. In accordance with our obligations under a stock purchase agreement executed in connection with the private placement, we have filed a registration statement on Form S-3 with the Securities and Exchange Commission for the purposes of registering for resale these shares, which has been declared effective by the SEC, pursuant to which such shares can be freely sold and traded. If the holders of a significant number of shares our common stock 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 equity awards can be freely sold in the public market upon issuance, subject to volume, notice and manner of sale limitations applicable to affiliates.

***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 common stock at a discount pursuant to our Employee Stock Purchase Plan.

In addition, the pre-funded warrants that we issued in connection with our December 2019 and June 2020 public offerings 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. To date, pre-funded warrants representing approximately 2.5 million shares of common stock have been exercised and as of March 31, 2021, pre-funded warrants representing 3,164,280 shares of common stock remain outstanding.

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 common stock. 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 significant 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. 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. To achieve compliance with Section 404, we must document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources and engage outside consultants to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. There is a risk that our internal control over financial reporting may, in the future, be found to be ineffective under Section 404. Our identification of one or more material weaknesses could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

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

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

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

### **Recent Sales of Unregistered Securities**

We did not sell any unregistered equity securities during the period covered by this Quarterly Report on Form 10-Q.

### **Purchase of Equity Securities**

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

## **Item 5. Other Information**

None.

## **Item 6. Exhibits and Financial Statement Schedules**

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

### **(2) Financial Statement Schedules**

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

**(3) Exhibits**

<b>Exhibit Number</b>	<b>Description of Exhibit</b>
<a href="#">3.1</a>	<a href="#">Restated Certificate of Incorporation of the Registrant, as amended April 16, 2019 (incorporated by reference to Exhibit 3.1 of the Registrant's Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 4, 2021)</a>
<a href="#">3.2</a>	<a href="#">Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.4 to Amendment No. 2 of the Registrant's Registration Statement on Form S-1 (File No. 333-190643) filed with the Securities and Exchange Commission on September 9, 2013)</a>
<a href="#">10.1</a>	<a href="#">Amendment No. 2 to the 2019 Inducement Stock Incentive Plan of the Registrant (incorporated by reference to Exhibit 10.12 of the Registrant's Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 4, 2021)</a>
<a href="#">10.2</a>	<a href="#">Amendment No. 2 to the Non-Employee Director Compensation Policy of the Registrant</a>
<a href="#">10.3</a>	<a href="#">Sales Agreement, dated March 4, 2021, between Cowen and Company, LLC and the Registrant (incorporated by reference to Exhibit 1.2 to the Registrant's Registration Statement on Form S-3 filed with the Securities and Exchange Commission on March 5, 2021)</a>
<a href="#">10.4</a>	<a href="#">Retirement and Consulting Agreement, dated April 4, 2021, between David R. Guyer, M.D. and the Registrant (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed with the Securities and Exchange Commission on April 5, 2021)</a>
<a href="#">31.1</a>	<a href="#">Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended</a>
<a href="#">31.2</a>	<a href="#">Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended</a>
<a href="#">32.1</a>	<a href="#">Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002</a>
<a href="#">32.2</a>	<a href="#">Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002</a>
101.INS*	Inline XBRL Instance Document
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Presentation Linkbase Document
104*	The cover page from this Quarterly Report on Form 10-Q, formatted in Inline XBRL

\*

Submitted electronically herewith.

Attached as Exhibit 101 to this report are the following formatted in XBRL (Extensible Business Reporting Language): (i) Condensed Consolidated Balance Sheets at March 31, 2021 (unaudited) and December 31, 2020, (ii) Condensed Consolidated Statements of Operations and Comprehensive Loss (unaudited) for the three month periods ended March 31, 2021 and 2020, (iii) Condensed Consolidated Statements of Stockholders' Equity (unaudited) for the three month periods ended March 31, 2021 and 2020, (iv) Condensed Consolidated Statements of Cash Flows (unaudited) for the three month periods ended March 31, 2021 and 2020 and (v) Notes to Condensed Financial Statements (unaudited).

**SIGNATURES**

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

**IVERIC bio, Inc.**

Date: May 5, 2021

By: /s/ David F. Carroll  
David F. Carroll  
Chief Financial Officer  
(Principal Financial and Accounting Officer)

AMENDMENT NO. 2 TO  
NON-EMPLOYEE DIRECTOR COMPENSATION POLICY  
OF  
IVERIC BIO, INC.

The Non-Employee Director Compensation Policy (the “Policy”) of IVERIC bio, Inc. (the “Company”) is hereby amended as follows (all capitalized terms used and not defined herein shall have the respective meanings ascribed to such terms in the Policy):

1. The section in the Policy captioned “Cash Compensation” under the heading in the Policy captioned “Non-Employee Director Compensation” be and hereby is deleted in its entirety and the following is inserted in lieu thereof:

***Cash Compensation***

The cash fees to be paid to non-employee directors for service on the Board, for service on each committee of the Board on which the director is then a member and for service in such additional Board positions as are described below shall be as follows:

- each non-employee director is eligible to receive an annual fee of \$45,000;
- the chair of the audit committee is eligible to receive an additional annual fee of \$20,000, and the other members of the audit committee are eligible to receive an additional annual fee of \$10,000;
- the chair of the compensation committee is eligible to receive an additional annual fee of \$17,500, and the other members of the compensation committee are eligible to receive an additional annual fee of \$10,000;
- the chair of the nominating and corporate governance committee is eligible to receive an additional annual fee of \$10,000, and the other members of the nominating and corporate governance committee are eligible to receive an additional annual fee of \$5,000;
- the chair of the R&D committee is eligible to receive an additional annual fee of \$10,000, and the other members of the R&D Committee are eligible to receive an additional annual fee of \$5,000; and
- the Independent Lead Director is eligible to receive an additional annual fee of \$25,000.

The foregoing fees are payable in arrears in four equal quarterly installments on the last day of each quarter, with such installments to be paid for any quarter during which the director served on the Board, on such committee or in such position.

In addition to the above fees, the Board may determine that additional committee fees are appropriate and should be payable for any newly created committee of the Board. The Board also may determine that an additional fee is appropriate and shall be payable to a non-employee Chairman of the Board, if one is then appointed. Consistent with this Policy, in determining any such additional fees, the Board will be guided by compensation paid to non-employee directors of a peer group of companies as well as current best practices.

2. Except as set forth herein, the Plan shall remain in full force and effect.

\* \* \*

*Approved by the Board of Directors on February 24, 2021.*

## CERTIFICATIONS

I, Glenn P. Sblendorio, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q for the quarter ended March 31, 2021 of IVERIC bio, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 5, 2021

By: /s/ Glenn P. Sblendorio  
Glenn P. Sblendorio  
Chief Executive Officer  
(Principal Executive Officer)

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## CERTIFICATIONS

I, David F. Carroll, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q for the quarter ended March 31, 2021 of IVERIC bio, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 5, 2021

By: /s/ David F. Carroll  
David F. Carroll  
Chief Financial Officer  
(Principal Financial Officer)

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

In connection with the Quarterly Report on Form 10-Q of IVERIC bio, Inc. (the "Company") for the period ended March 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Glenn P. Sblendorio, Chief Executive Officer of the Company, hereby certifies, pursuant to Rule 13a-14(b) and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to his knowledge:

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

Date: May 5, 2021

By: /s/ Glenn P. Sblendorio  
Glenn P. Sblendorio  
Chief Executive Officer  
*(Principal Executive Officer)*

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