

APPLIED GENETIC TECHNOLOGIES CORP

Form S-1/A

March 04, 2014

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As filed with the Securities and Exchange Commission on March 4, 2014.

Registration No. 333-193309

**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

**Amendment No. 1**  
**to**  
**FORM S-1**  
**REGISTRATION STATEMENT**

*under*

*THE SECURITIES ACT OF 1933*

**APPLIED GENETIC TECHNOLOGIES CORPORATION**

(Exact Name of Registrant as Specified in Its Charter)

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<b>Delaware</b> (State or Other Jurisdiction of Incorporation or Organization)	<b>2836</b> (Primary Standard Industrial Classification Code No.) <b>11801 Research Drive, Suite D</b>	<b>59-3553710</b> (I.R.S. Employer Identification No.)
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**Alachua, Florida 32615**

**(386) 462-2204**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**Susan B. Washer**

**President and Chief Executive Officer**

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**Alachua, Florida 32615**

**(386) 462-2204**

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**Approximate date of commencement of proposed sale to the public:** As soon as practicable after this Registration Statement is declared effective.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended (the "Securities Act") please check the following box. "

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. "

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. "

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. "

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b2 of the Exchange Act.

Large accelerated filer "

Accelerated filer "

Non-accelerated filer  (Do not check if a smaller reporting company)

Smaller reporting company "

**The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.**

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The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell nor does it seek an offer to buy these securities in any state where the offer or sale is not permitted.

**Subject to Completion, dated March 4, 2014**

**PROSPECTUS**

**Shares**

**Common Stock**

**Applied Genetic Technologies Corporation**

March , 2014.

This is the initial public offering of the common stock of Applied Genetic Technologies Corporation. We anticipate that the initial public offering price will be between \$ and \$ per share.

We have granted the underwriters the option to purchase additional shares of common stock to cover over-allotments.

We have applied to list our shares of common stock on the NASDAQ Global Market under the symbol AGTC.

**Investing in our common stock involves risks. See Risk Factors beginning on page 12 of this prospectus.**

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

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

	<b>Per share</b>	<b>Total</b>
Initial public offering price	\$	\$
Underwriting discounts and commissions (1)	\$	\$
Proceeds to AGTC (before expenses)	\$	\$

(1) We refer you to Underwriting beginning on page 158 of this prospectus for additional information regarding total underwriter compensation.

The underwriters expect to deliver the shares to purchasers on or about \_\_\_\_\_, 2014 through the book-entry facilities of The Depository Trust Company.

**BMO Capital Markets    Wedbush PacGrow Life Sciences**

**Cantor Fitzgerald & Co.    Roth Capital Partners**

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**You should rely only on the information contained in this prospectus and any free writing prospectus prepared by us or on our behalf or to which we have referred you. We and the underwriters have not authorized anyone to provide you with information that is different. We and the underwriters are offering to sell shares of our common stock, and seeking offers to buy shares of our common stock, only in jurisdictions where such offers and sales are permitted. Regardless of the time of delivery of this prospectus or any free writing prospectus or any sale of our common stock, the information in this prospectus is accurate only as of the date of this prospectus, and the information in any free writing prospectus that we may provide you in connection with this offering is accurate only as of the date of that free writing prospectus. Our business, financial condition, results of operations and future growth prospects may have changed since those dates.**

**Until , 25 days after the date of this prospectus, all dealers that buy, sell or trade our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This requirement is in addition to the dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to unsold allotments or subscriptions.**

For investors outside the United States: Neither we nor any of the underwriters have taken any action to permit a public offering of the shares of our common stock or the possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus and any free writing prospectus outside of the United States.

Estimates in this prospectus of the patient populations for the diseases that we are targeting are based on published estimates of the rates of incidence of the diseases from scientific and general publications and research, surveys and studies conducted by third parties that we consider to be reliable, although such publications do not guarantee the accuracy or completeness of such information. We assume populations of approximately 300 million persons in the United States and approximately 500 million persons in Europe.

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### PROSPECTUS SUMMARY

*This summary highlights information contained elsewhere in this prospectus. You should read the following summary together with the more detailed information appearing in this prospectus, including our financial statements and related notes and the risk factors beginning on page 12 before deciding whether to purchase shares of our common stock. Unless the context otherwise requires, we use the terms "AGTC," "Company," "we," "us" and "our" in this prospectus to refer to Applied Genetic Technologies Corporation.*

#### Overview

We are a clinical-stage biotechnology company that uses our proprietary gene therapy platform to develop products designed to transform the lives of patients with severe inherited orphan diseases in ophthalmology. Our lead product candidates, which are each in the preclinical stage, focus on rare diseases of the eye, caused by mutations in single genes, that significantly affect visual function and currently lack effective medical treatments. We have also obtained preliminary evidence of the safety and efficacy of our gene therapy approach in clinical-stage programs involving other diseases outside our current area of focus that we believe provide proof of concept for our gene therapy platform.

Our gene therapy approach uses a viral vector to deliver a functional copy of a gene to the patient's own cells through a variety of delivery methods. A viral vector is a virus that has been modified to carry a gene and deliver it to a cell. Our viral vectors utilize a modified version of a non-replicating strain of virus known as an adeno-associated virus, or AAV, which is incapable of causing disease in humans. When an AAV vector containing a functional copy of a gene is administered, the functional genetic material resides in the nucleus of the patient's cell, providing safe, sustained expression of the therapeutic protein to treat the disease without modifying the existing DNA of the patient.

We have developed extensive internal expertise in viral vector design, delivery and manufacturing that is supported by a broad intellectual property estate. Our proprietary AAV vector manufacturing process is both reproducible and scalable. We have assembled an experienced management team and a world-class group of scientific advisors, and we have strong collaborative relationships with key opinion leaders in the field of gene therapy. Combining these attributes, we have built a gene therapy platform that we believe will provide patients with treatments that may have life-long clinical benefits, potentially based on a one-time therapeutic administration.

#### Our product pipeline

Our lead product candidates are designed to treat:

**X-linked retinoschisis, or XLRS.** XLRS is an inherited retinal disease caused by mutations in the RS1 gene, which encodes the retinoschisin protein. It is characterized by abnormal splitting of the layers of the retina, resulting in poor visual acuity in young boys, which can progress to legal blindness in adult men. In preclinical studies, treatment by injection of our XLRS product candidate in mice improved responses to light in the retina and visual acuity. In late 2014, we plan to submit an Investigational New Drug Application, or IND, to the United States Food and Drug Administration, or FDA, and to initiate a Phase 1/2 clinical trial in XLRS, with initial clinical data expected in mid-2015.

**Achromatopsia, or ACHM.** ACHM is an inherited retinal disease, which is present from birth and is characterized by the lack of cone photoreceptor function. The condition results in markedly reduced visual acuity, light sensitivity, day blindness and complete loss of color discrimination. Best-corrected visual acuity in persons affected by ACHM, even under subdued light conditions, is usually about 20/200, a level at which people are considered legally blind. Preclinical studies in both mouse and dog models of our

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ACHM product candidate have shown the ability to restore photoreceptor function, improve visual acuity and mitigate light sensitivity and day blindness. In early 2015, we plan to submit an IND and to initiate a Phase 1/2 clinical trial in one form of ACHM, with initial clinical data expected in late 2015.

**X-linked retinitis pigmentosa, or XLRP.** XLRP is an inherited retinal dystrophy characterized by the progressive loss of vision, one form of which is caused by mutations in the RPGR gene, which encodes a protein essential for normal vision. It is commonly first observed in young men, who notice problems with vision under low light conditions, or night blindness, followed by tunnel vision, leading to poor central vision and eventual total blindness. A preclinical study in a dog model of XLRP caused by mutations in the RPGR gene demonstrated a delay in the rate of disease progression in dogs that received a subretinal injection of our XLRP product candidate.

We initially developed our gene therapy platform in clinical-stage proof-of-concept programs involving three other diseases:

Leber congenital amaurosis (type 2), or LCA2, an orphan eye disease caused by mutation in the RPE65 gene;

the wet form of age-related macular degeneration, or wet AMD, an eye disease affecting a large patient population; and

Alpha-1 antitrypsin deficiency, or AAT deficiency, an inherited orphan lung disease.

While not our principal focus at this time, these proof-of-concept programs are important because they have provided initial evidence of safety and efficacy of our gene therapy approach in both preclinical studies and clinical trials. They have also enabled us to develop substantial experience in vector design, delivery and manufacturing, clinical trial design and conduct, and in working with clinical investigators and regulatory agencies. In these proof-of-concept programs, our manufacturing process has been successfully vetted by regulatory agencies and partners and we have demonstrated our ability to produce clinical material for multiple studies.

In clinical trials conducted by our licensee Genzyme Corporation, or Genzyme, up to 34 patients with wet AMD were treated by intravitreal injection of an AAV vector, and in other trials conducted by us and others, more than 50 patients with LCA2 have been treated with subretinal injections of AAV vectors, in both cases without reports of serious adverse events attributed to the vector, and with promising indications of efficacy for LCA2 patients. See [Business Strategic collaborations Our license to Genzyme](#). We believe our AAT deficiency program provides proof of concept for the use of our gene therapy platform in indications outside our focus area of orphan ophthalmology. We have conducted Phase 1 and Phase 2 clinical trials for our AAT deficiency product candidate in 30 patients and expect to start a Phase 2b trial in early 2015, with initial clinical data expected in mid-2015.



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The chart below summarizes our current gene therapy programs:

### **Our gene therapy platform**

Our gene therapy platform is built on our core competencies in three key areas: vector selection and design, vector manufacturing and vector delivery:

*Vector selection and design.* The success of a gene therapy platform is highly dependent on the vector selected. Our gene therapy platform is based on viral vectors that utilize a modified version of the non-replicating adeno-associated virus to deliver a functional copy of a gene to the patient's own cells. We believe that AAV vectors are particularly well-suited for treating our target diseases and offer advantages including safety, stability and sustained expression compared with viral vectors such as adenovirus, herpes virus and lentivirus used by others. AAV vectors can carry genes of up to 4,000 base pairs in length, a carrying capacity sufficient to accommodate more than 90% of human genes.

One of our key capabilities is our understanding of the complex interplay between the clinical disease, the cells in the patient's body that need treatment, the selection of the protein shell, or capsid, and a promoter, the design of the gene construct and the physical administration method. We have spent years

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conducting research on the best combinations of these elements with the aim of developing safe and effective gene therapy treatments.

*Vector manufacturing.* We have developed a proprietary, high-yield vector manufacturing process using scalable technologies, which addresses problems of low productivity and low efficacy that have historically plagued efforts to manufacture AAV vectors and enables us to produce vectors with improved potency, efficiency and safety over processes previously used by us and others.

Our manufacturing process has been reviewed by both the FDA and the European Medicines Agency, or EMA, has been authorized for production of product candidates for use in clinical trials in the United States and Europe and has been transferred successfully to Genzyme and to our contract manufacturing organization. We hold or have licensed 80 issued and 28 pending patents covering our manufacturing technology. We believe that our core competency and intellectual property estate in vector manufacturing differentiate us competitively and provide a key element of our gene therapy platform.

*Vector delivery.* Our gene therapy platform allows for vector delivery by a variety of methods, and we select the method that is most beneficial for the disease we are targeting. In ophthalmology, the product candidate can best be delivered to cells in the eye by injection. For other indications, such as AAT deficiency, we plan to administer the product candidate by intramuscular injection or vascular delivery. These methods of administration are well-established for the safe and effective delivery of other drugs and protein products.

Because our AAV vectors can be used to introduce functional genes into many different cell types and by a variety of delivery methods and have a carrying capacity sufficient to accommodate most of the individual genes in the human genome, our gene therapy platform has the potential to provide treatments for many other diseases outside of our current focus on orphan ophthalmology, including those with large dosing requirements or in larger markets. We have already conducted preclinical proof-of-concept studies and Phase 1 and Phase 2 clinical trials of a treatment for AAT deficiency. We expect to explore other therapeutic areas selectively, either alone or through partnerships.

### **Our focus on orphan ophthalmology**

We focus on orphan ophthalmology because we believe there is a significant unmet medical need in orphan eye diseases that provides an attractive business opportunity. The prevalence of the diseases we are pursuing is large by orphan standards, but small enough to permit clinical trials on a manageable scale and to provide markets that we believe can be served using a small, targeted commercial infrastructure. The eye diseases we are targeting are also of interest to us due to a number of factors that have enabled us to predict the potential safety and efficacy of our product candidates at an early stage of development:

these diseases involve well-understood disease mechanisms;

these are monogenic diseases, meaning they are caused by mutations in a single gene, which mitigates the uncertainty of disease biology;

highly predictive animal models are available;

local delivery of the therapeutic agent is possible via methods already widely used in ophthalmology;

these diseases have clearly defined clinical endpoints that have been accepted by regulatory agencies in review of other ophthalmology products; and

we anticipate a short time to meaningful clinical data.

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### **Our strategy**

Our objective is to become the world leader in developing and commercializing gene therapy treatments for inherited orphan diseases in ophthalmology, for which there are no currently available treatments, and to thereby provide a better life for people with these diseases. Our strategy to accomplish this goal is to:

develop and commercialize drugs in orphan ophthalmology;

continue our leadership position in orphan ophthalmology;

extend our expertise in AAV vector selection and design, delivery and manufacturing;

pursue monogenic orphan indications with high unmet medical need and greater probability of clinical, regulatory and commercial success; and

develop and partner selectively to expand the scope of our pipeline and the utilization of our gene therapy platform.

### **Risks associated with our business**

Our ability to implement our business strategy is subject to numerous risks that you should be aware of before making an investment decision. These risks are described more fully in the section entitled "Risk Factors" beginning on page 12 of this prospectus. You are encouraged to read that section in its entirety before making an investment decision. These risks include, but are not limited to, the following:

We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.

Our ability to generate revenue from product sales is highly uncertain and we may never achieve or sustain profitability.

In order to obtain regulatory approval for and commercialize our product candidates we will need to raise additional funding in the future, which may not be available on acceptable terms, or at all.

All of our product candidates are in preclinical or clinical development. Clinical drug development is expensive, time consuming and uncertain, and we may ultimately not be able to obtain regulatory approvals for the commercialization of some or all of our product candidates.

Our gene therapy product candidates are based on a novel technology, no gene therapy products have been approved in the United States and only one such product has been approved in Europe, which makes it difficult to predict the time and cost of product candidate development and regulatory approval.

Success in animal studies or early clinical trials may not be indicative of results obtained in later trials.

We may encounter substantial delays in our clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

Even if we complete the necessary clinical trials, we cannot predict when or if we will obtain regulatory approval to commercialize a product candidate or the approval may be for a more narrow indication than we expect.

We expect to rely on third parties to conduct, supervise and monitor our clinical trials and to conduct certain aspects of our product manufacturing and protocol development, and if these third parties perform in an unsatisfactory manner, it may harm our business.

The insurance coverage and reimbursement status of our product candidates is uncertain, and failure to obtain or maintain adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue.

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Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of our product candidates or adversely affect our ability to conduct our business, raise additional funding, obtain regulatory approvals or achieve market acceptance for our product candidates.

If we are unable to obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained 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 impaired.

### **Corporate information**

We were incorporated in Florida in January 1999 and reincorporated in Delaware in October 2003. Our principal executive offices are located at 11801 Research Drive, Suite D, Alachua, Florida 32615, and our telephone number is (386) 462-2204. Our corporate website address is [www.agtc.com](http://www.agtc.com). Information contained on or accessible through our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is an inactive textual reference only.

We use AGTC and the double helix logo as trademarks in the United States and other countries. We have begun the registration process for these trademarks in the United States.

This prospectus contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to in this prospectus, including logos, artwork, and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any such companies.

### **Implications of being an emerging growth company**

As a company with less than \$1 billion in revenue during our last fiscal year, we qualify as an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced Management's Discussion and Analysis of Financial Condition and Results of Operations disclosure;

reduced disclosure about our executive compensation arrangements;

no non-binding advisory votes on executive compensation or golden parachute arrangements; and

exemption from the auditor attestation requirement in the assessment of our internal controls over financial reporting.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than \$1 billion in annual revenue, we have more than \$700 million in market value of our stock held by non-affiliates or we issue more than \$1 billion of non-convertible debt over a three-year period. We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of certain reduced reporting burdens in this prospectus. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

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In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

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**The Offering**

Common stock offered by AGTC	shares
Common stock to be outstanding after this offering	shares ( shares in the event the underwriters elect to exercise in full their over-allotment option to purchase additional shares from us)
Use of proceeds	We estimate that the net proceeds from this offering will be approximately \$ million, or approximately \$ million if the underwriters exercise in full their over-allotment option, based on the initial public offering price of \$ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. We plan to use the net proceeds from this offering to extend development of our XLRS and ACHM product candidates beyond Phase 1/2 trials (which we believe are already adequately funded), and if successful to initiate pivotal Phase 3 trials for these product candidates, to continue preclinical studies of our XLRP product candidate and to explore in early preclinical studies potential applications of our gene therapy platform in other indications in orphan ophthalmology. We intend to use remaining amounts for working capital and other general corporate purposes. We may also use a portion of the net proceeds to in-license, acquire or invest in complementary gene therapy businesses, technologies, products or assets, as well as to selectively explore potential applications of our gene therapy platform in indications outside of orphan ophthalmology. See Use of Proceeds.
Risk factors	You should read the Risk Factors section and other information included in this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Proposed NASDAQ Global Market symbol	AGTC

The number of shares of our common stock to be outstanding after this offering set forth above is based on the 109,039 shares of our common stock outstanding as of December 31, 2013 and assumes the conversion of all outstanding shares of our preferred stock into 9,120,081 shares of common stock upon the closing of this offering.

The number of shares of common stock to be outstanding after this offering excludes:

59,247 shares of common stock issuable upon the exercise of preferred stock warrants outstanding as of December 31, 2013, at a weighted average exercise price of \$13.64 per share;

782,965 shares of common stock issuable upon the exercise of stock options outstanding under our 2001 Stock Option Plan and our 2011 Stock Incentive Plan as of December 31, 2013, at a weighted average exercise price of \$3.23 per share;

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185,140 shares of common stock available for future issuance under our 2001 Stock Option Plan and our 2011 Stock Incentive Plan as of December 31, 2013; and

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an additional 1,279,999 shares of our common stock that will be made available for future issuance under our equity compensation plans upon the closing of this offering.

Except as otherwise noted, all information in this prospectus:

gives effect to a 1-for-35 reverse split of our common stock effected on March 4, 2014;

assumes no exercise of outstanding options or warrants described above;

assumes no exercise by the underwriters of their over-allotment option to purchase additional shares of common stock from us;

gives effect to the automatic conversion of all outstanding shares of our preferred stock into 9,120,081 shares of our common stock upon the closing of this offering; and

gives effect to the amendment and restatement of our certificate of incorporation and bylaws upon the closing of this offering.

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The following summary financial data should be read together with our financial statements and accompanying notes and Management's Discussion and Analysis of Financial Condition and Results of Operations appearing elsewhere in this prospectus. Our summary statement of operations data for the fiscal years ended June 30, 2012 and 2013 and our summary balance sheet data as of June 30, 2012 and 2013 are derived from our audited financial statements included elsewhere in this prospectus. Our summary statement of operations data for the six months ended December 31, 2012 and 2013 and our summary balance sheet data as of December 31, 2013 have been derived from our unaudited financial statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of results to be expected for any future period, and our interim results are not necessarily indicative of our results for the entire year or any future period. The summary financial data in this section are not intended to replace our financial statements and the related notes.

The pro forma balance sheet data as of December 31, 2013 gives effect to the conversion of all of our preferred stock into 9,120,081 shares of common stock upon the closing of this offering and the conversion of all outstanding warrants exercisable for shares of Series A-1, Series A-1A and Series B-1 preferred stock into warrants exercisable for shares of common stock, resulting in our preferred stock warrant liability being reclassified to additional paid-in capital. The pro forma as adjusted balance sheet data as of December 31, 2013 gives effect to (1) the pro forma adjustments described above and (2) our receipt of estimated net proceeds of \$        million from this offering, based on the initial public offering price of \$        per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and estimated offering expenses payable by us, as if each had occurred as of December 31, 2013. The pro forma as adjusted summary financial data are not necessarily indicative of what our financial position would have been if this offering had been completed as of the date indicated, nor are these data necessarily indicative of our financial position for any future date or period.

	Fiscal Year Ended June 30,		Six Months Ended December 31,	
	2012	2013	2012	2013
(in thousands except per share data)				
<b>Statement of Operations Data:</b>				
Revenue:				
Grant revenue	\$ 718	\$ 439	\$ 293	\$ 466
Sponsored research revenue	364	503	156	307
<b>Total revenue</b>	<b>1,082</b>	<b>942</b>	<b>449</b>	<b>773</b>
Operating expenses:				
Research and development	2,354	3,133	1,156	3,673
General and administrative	787	1,403	649	1,971
<b>Total operating expenses</b>	<b>3,141</b>	<b>4,536</b>	<b>1,805</b>	<b>5,644</b>
Loss from operations	(2,059)	(3,594)	(1,356)	(4,871)

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	Fiscal Year Ended		Six Months Ended	
	June 30, 2012	2013	December 31, 2012	2013
	(in thousands except per share data)			
Other income (expense):				
Interest income		10		15
Interest expense	(69)	(191)	(152)	
Fair value adjustments to warrant liabilities (1)	204	(8)	5	(105)
Fair value adjustments to Series B purchase rights (1)		(1,207)	(437)	(2,838)
Total other income (expense), net	135	(1,396)	(584)	(2,928)
Net loss	\$ (1,924)	\$ (4,990)	\$ (1,940)	\$ (7,799)
Net loss per share, basic and diluted (2)	\$ (17.65)	\$ (45.78)	\$ (17.80)	\$ (71.55)
Weighted-average shares outstanding, basic and diluted (2)	109	109	109	109
Pro forma net loss per share, basic and diluted (unaudited) (2)		\$ (1.20)		\$ (1.13)
Weighted-average pro forma shares outstanding, basic and diluted (unaudited) (2)		4,146		6,885

	As of June 30,		As of December 31,		Pro Forma As Adjusted (3)
	2012	2013	2013	2013	
			Actual (in thousands)	Pro Forma	
<b>Balance Sheet Data:</b>					
Cash and cash equivalents	\$ 774	\$ 8,893	\$ 8,998	\$ 8,998	\$
Short-term investments	\$	\$ 14,000	\$ 19,000	\$ 19,000	\$
Working capital	\$ (399)	\$ 20,051	\$ 28,106	\$ 28,106	\$
Total assets	\$ 2,824	\$ 25,490	\$ 31,709	\$ 31,709	\$
Current liabilities	\$ 1,494	\$ 3,460	\$ 1,644	\$ 1,644	\$
Total stockholders (deficit) equity	\$ (31,290)	\$ (36,183)	\$ (43,871)	\$ 30,065	\$

- (1) See note 6 of the notes to financial statements appearing elsewhere in this prospectus for a description of the fair value adjustments to our warrant liabilities and Series B purchase rights.
- (2) See note 2 of the notes to financial statements appearing elsewhere in this prospectus for a description of the method used to calculate basic and diluted net loss per share and pro forma basic and diluted net loss per share.
- (3) A \$1.00 increase (decrease) in the assumed initial public offering price of \$ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets and total stockholders (deficit) equity by approximately \$ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, a one million share increase (decrease) in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) each of cash and cash equivalents, working capital, total assets and total stockholders equity (deficit) by \$ million, assuming the assumed initial public offering price of \$ per share (the midpoint of the price range set forth on the cover page of this prospectus) remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

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**RISK FACTORS**

*Investing in our common stock involves a high degree of risk. Before you decide to invest in our common stock, you should consider carefully the risks described below, together with the other information contained in this prospectus, including our financial statements and the related notes appearing at the end of this prospectus. We believe the risks described below are the risks that are material to us as of the date of this prospectus. If any of the following risks actually occur, our business, financial condition, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you may lose part or all of your investment.*

**Risks related to our financial condition and capital requirements**

*We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.*

We are a clinical-stage biotechnology company, and we have not yet generated revenues from product sales. We have incurred losses from operations in each year since our inception in 1999, and net losses of \$1.9 million and \$5.0 million for the years ended June 30, 2012 and 2013, respectively. As of December 31, 2013, we had an accumulated deficit of \$56.2 million. Our prior losses, combined with expected future losses, have had and may continue to have an adverse effect on our stockholders' equity and working capital.

We have devoted most of our financial resources to research and development, including our clinical and preclinical development activities. To date, we have financed our operations primarily through the sale of equity securities and, to a lesser extent, through research grants from third parties or milestone payments from a collaborator. The amount of our future net losses will depend, in part, on the rate of our future expenditures and our ability to obtain funding through equity or debt financings, strategic collaborations or additional grants. We have not begun clinical trials for our lead product candidates and it will be several years, if ever, before we have a product candidate ready for commercialization. Even if we obtain regulatory approval to market a product candidate, our future revenues will depend upon the size of any markets in which our product candidates have received approval, and our ability to achieve sufficient market acceptance, reimbursement from third-party payors and adequate market share for our product candidates in those markets.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

continue our research and preclinical and clinical development of our product candidates;

expand the scope of our current clinical trials for our product candidates;

initiate additional preclinical studies, clinical trials or other studies for our product candidates;

further develop our gene therapy platform, including the process for design, delivery and manufacturing of our vectors for our product candidates;

change or add additional manufacturers or suppliers;

seek regulatory and marketing approvals for our product candidates that successfully complete clinical trials;

establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;

seek to identify and validate additional product candidates;

acquire or in-license other product candidates and technologies;

make milestone or other payments under any in-license agreements;

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maintain, protect and expand our intellectual property portfolio;

attract and retain skilled personnel;

create additional infrastructure to support our operations as a public company and our product development and planned future commercialization efforts; and

experience any delays or encounter issues with any of the above.

The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

***Our ability to generate revenue from product sales is highly uncertain and we may never achieve or sustain profitability, which could depress the market price of our common stock, and could cause you to lose part or all of your investment.***

All of our revenue generated to date has come from research grants from third parties or license fees or milestone payments from a collaborator. Our ability to generate substantial revenue and achieve profitability depends on our ability, alone or with strategic collaboration partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, our product candidates. We do not anticipate generating revenues from product sales for at least the next several years, if ever. If any of our product candidates fail in clinical trials or do not gain regulatory approval, or if any of our product candidates, if approved, fail to achieve market acceptance, we may never become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our ability to generate future revenues from product sales depends heavily on our success in:

completing research and preclinical and clinical development of our product candidates;

seeking and obtaining regulatory and marketing approvals for product candidates for which we complete clinical trials;

establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate (in amount and quality) products and services to support clinical development and the market demand for our product candidates, if approved;

launching and commercializing product candidates for which we obtain regulatory and marketing approval, either by collaborating with a partner or, if launched independently, by establishing a sales, marketing and distribution infrastructure;

obtaining and maintaining adequate coverage and reimbursement from third-party payors for our product candidates;

obtaining market acceptance of our product candidates and gene therapy as a viable treatment option;

addressing any competing technological and market developments;

implementing additional internal systems and infrastructure, as needed;

identifying and validating new gene therapy product candidates;

negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter;

maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how; and

attracting, hiring and retaining qualified personnel.

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Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the FDA, the EMA or other regulatory agencies, domestic or foreign, to perform clinical trials and other studies in addition to those that we currently anticipate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations. Our failure to become and remain profitable would depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations.

***In order to obtain regulatory approval for and commercialize our product candidates, we will need to raise additional funding in the future, which may not be available on acceptable terms, or at all. Failure to obtain necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.***

All of our lead programs in orphan ophthalmology are currently in preclinical development. Developing gene therapy products is expensive, and we expect our research and development expenses to increase substantially as we advance our current product candidates in clinical trials and as we undertake preclinical studies of new product candidates.

Our operations have consumed substantial amounts of cash since inception. As of December 31, 2013, our cash and cash equivalents and short-term investments were \$28.0 million. Our research and development expenses were \$2.4 million and \$3.1 million for the fiscal years ended June 30, 2012 and 2013, respectively, and \$1.2 million and \$3.7 million for the six months ended December 31, 2012 and 2013, respectively. We estimate that the net proceeds from this offering will be approximately \$ , based on the initial public offering price of \$ , after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We expect that the net proceeds from this offering and our existing cash and cash equivalents will be sufficient to enable us to complete planned preclinical studies and clinical trials for our lead product candidates for at least the next 24 months. See Use of Proceeds. In order to complete the process of obtaining regulatory approval for our lead product candidates and to build the sales, marketing and distribution infrastructure that we believe will be necessary to commercialize our lead product candidates, if approved, we will require substantial additional funding. Also, our current operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or a combination of these approaches.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, financing may not be available to us in the future in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and a portion of our operating cash flows, if any, being dedicated to the payment of principal and interest on such indebtedness, and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or otherwise at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available, and we may be required to relinquish or license on unfavorable terms rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, financial condition, results of operations and prospects and cause the price of our common stock to decline.



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If we are unable to obtain needed funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidates or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition, results of operations and prospects and cause the price of our common stock to decline.

### **Risks related to the discovery and development of our product candidates**

*All of our product candidates are in preclinical or clinical development. Clinical drug development is expensive, time consuming and uncertain, and we may ultimately not be able to obtain regulatory approvals for the commercialization of some or all of our product candidates.*

The research, testing, manufacturing, labeling, approval, selling, marketing and distribution of drug products are subject to extensive regulation by the FDA and other regulatory authorities, which regulations differ from country to country. Our product candidates are in various stages of development and are subject to the risks of failure typical of drug development. The development and approval process is expensive and can take many years to complete, and its outcome is inherently uncertain. We have not submitted an application for or received marketing approval for any of our product candidates. We have limited experience in conducting and managing the later stage clinical trials necessary to obtain regulatory approvals, including approval by the FDA. To receive approval, we must, among other things, demonstrate with substantial evidence from clinical trials that the product candidate is both safe and effective for each indication for which approval is sought, and failure can occur in any stage of development. Satisfaction of the approval requirements typically takes several years and the time needed to satisfy them may vary substantially, based on the type, complexity and novelty of the pharmaceutical product. We cannot predict if or when we might receive regulatory approvals for any of our product candidates currently under development.

The FDA and foreign regulatory authorities also have substantial discretion in the drug approval process. The number and types of preclinical studies and clinical trials that will be required for regulatory approval varies depending on the product candidate, the disease or condition that the product candidate is designed to address, and the regulations applicable to any particular product candidate. Approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, and there may be varying interpretations of data obtained from preclinical studies or clinical trials, either of which may cause delays or limitations in the approval or the decision not to approve an application. Regulatory agencies can delay, limit or deny approval of a product candidate for many reasons, including:

the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;

we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;

the results of clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory authorities for approval;

the patients recruited for a particular clinical program may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;

the results may not confirm the positive results from earlier preclinical studies or clinical trials;

we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;

the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;

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the data collected from clinical trials of our product candidates may not be sufficient to the satisfaction of FDA or comparable foreign regulatory authorities to support the submission of a biologics license application, or BLA, or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere;

regulatory agencies might not approve or might require changes to our manufacturing processes or facilities; or

regulatory agencies may change their approval policies or adopt new regulations in a manner rendering our clinical data insufficient for approval.

Any delay in obtaining or failure to obtain required approvals could materially adversely affect our ability to generate revenue from the particular product candidate, which likely would result in significant harm to our financial position and adversely impact our stock price. Furthermore, any regulatory approval to market a product may be subject to limitations on the indicated uses for which we may market the product. These limitations may limit the size of the market for the product.

We are not permitted to market our product candidates in the United States or in other countries until we receive approval of a BLA from the FDA or marketing approval from applicable regulatory authorities outside the United States. Obtaining approval of a BLA can be a lengthy, expensive and uncertain process. If we fail to obtain FDA approval to market our product candidates, we will be unable to sell our product candidates in the United States, which will significantly impair our ability to generate any revenues. In addition, failure to comply with FDA and non-U.S. regulatory requirements may, either before or after product approval, if any, subject our company to administrative or judicially imposed sanctions, including:

restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;

restrictions on the products, manufacturers or manufacturing process;

warning letters;

civil and criminal penalties;

injunctions;

suspension or withdrawal of regulatory approvals;

product seizures, detentions or import bans;

voluntary or mandatory product recalls and publicity requirements;

total or partial suspension of production;

imposition of restrictions on operations, including costly new manufacturing requirements; and

refusal to approve pending BLAs or supplements to approved BLAs.

Even if we do receive regulatory approval to market a product candidate, any such approval may be subject to limitations on the indicated uses for which we may market the product. It is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain the appropriate regulatory approvals necessary for us or our collaborators to commence product sales. Any delay in obtaining, or an inability to obtain, applicable regulatory approvals would prevent us from commercializing our product candidates, generating revenues and achieving and sustaining profitability.

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*Our gene therapy product candidates are based on a novel technology, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval. At the moment, no gene therapy products have been approved in the United States and only one such product has been approved in Europe.*

We have concentrated our product research and development efforts on our gene therapy platform, and our future success depends on the successful development of this approach. There can be no assurance that any development problems we experience in the future related to our gene therapy platform will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience unanticipated problems or delays in expanding our manufacturing capacity or transferring our manufacturing process to commercial partners, which may prevent us from completing our clinical trials or commercializing our products on a timely or profitable basis, if at all.

In addition, the clinical trial requirements of the FDA, the EMA and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of such product candidates. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or extensively studied pharmaceutical or other product candidates. At the moment, only one gene therapy product, UniQure's Glybera, which received marketing authorization from the EMA in 2012, has been approved in Europe but has not yet been launched for commercial sale, which makes it difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in either the United States or Europe. Approvals by the EMA may not be indicative of what the FDA may require for approval.

Regulatory requirements governing gene and cell therapy products have changed frequently and may continue to change in the future. For example, the FDA has established the Office of Cellular, Tissue and Gene Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the United States National Institutes of Health, or the NIH, are also subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee, or the RAC. Although the FDA decides whether individual gene therapy protocols may proceed, the RAC review process can delay the initiation of a clinical trial, even if the FDA has reviewed the trial design and details and approved its initiation. Conversely, the FDA can put an IND on clinical hold even if the RAC has provided a favorable review of the drug. Also, before a clinical trial can begin at an NIH-funded institution, that institution's institutional review board, or IRB, and its Institutional Biosafety Committee have to review the proposed clinical trial to assess the safety of the trial. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other regulatory bodies to change the requirements for approval of any of our product candidates.

These regulatory review committees and advisory groups and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, 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. As we advance our product candidates, we will be required to consult with these regulatory and advisory groups, and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of our product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected for orphan ophthalmology product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue to maintain our business.

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### ***Success in animal studies or early clinical trials may not be indicative of results obtained in later trials.***

Trial designs and results from animal studies or previous clinical trials are not necessarily predictive of our future clinical trial designs or results, and interim results of a clinical trial are not necessarily indicative of final results. Our product candidates may also fail to show the desired safety and efficacy in clinical development despite demonstrating positive results in animal studies or having successfully advanced through initial clinical trials. For example, our animal studies of our AAT product candidate resulted in evidence of significant production of AAT levels, but early clinical trials of our product candidate showed significantly lower levels of AAT production in treated patients. There can be no assurance that the success we achieved in the animal studies for our lead product candidates will result in success in our clinical trials of those product candidates.

There is a high failure rate for drugs and biological products proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials even after achieving promising results in earlier stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including due to changes in regulatory policy during the period of our product candidate development.

### ***We may find it difficult to enroll patients in our clinical trials, which could delay or prevent clinical trials of our product candidates.***

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of our clinical trials depends on the speed at which we can recruit patients to participate in testing our product candidates as well as completion of required follow-up periods. If patients are unwilling to participate in our gene therapy studies because of negative publicity from adverse events in the biotechnology or gene therapy industries or for other reasons, including competitive clinical trials for similar patient populations, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of our product candidates may be delayed. For example, trials using early versions of lentiviral vectors, which integrate with, and thereby alter, the host cell's DNA, have led to several well-publicized adverse events, including reported cases of leukemia. If there are delays in accumulating the required number of clinical events in trials for our product candidates where clinical events are a primary endpoint, there may be delays in completing the trial. These delays could result in increased costs, delays in advancing our product candidates, delays in testing the effectiveness of our technology or termination of the clinical trials altogether.

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics to achieve diversity in a trial, to complete our clinical trials in a timely manner. In particular, each of the conditions for which we plan to evaluate our product candidates are rare genetic disorders with limited patient pools from which to draw for clinical trials. The eligibility criteria of our clinical trials will further limit the pool of available trial participants.

Patient enrollment is affected by factors including:

severity of the disease under investigation;

design of the clinical trial protocol;

size and nature of the patient population;

eligibility criteria for the trial in question;

perceived risks and benefits of the product candidate under trial;

proximity and availability of clinical trial sites for prospective patients;

availability of competing therapies and clinical trials;

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clinicians and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating;

efforts to facilitate timely enrollment in clinical trials;

patient referral practices of physicians; and

our ability to monitor patients adequately during and after treatment.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may be forced to delay, limit or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business. We could encounter delays if physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of our product candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles.

We plan to seek initial marketing approval for our product candidates in the United States and the European Economic Area, or EEA. We may not be able to initiate or continue clinical trials if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by the FDA, the EMA or other foreign regulatory authorities. Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

difficulty in establishing or managing relationships with contract research organizations, or CROs, and physicians;

different standards for conducting clinical trials;

our inability to locate qualified local consultants, physicians and partners; and

the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatments.

***We may encounter substantial delays in our clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.***

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of such product candidates in humans. Clinical testing is expensive, time-consuming and uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical trials can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development include:

delays in raising, or inability to raise, sufficient capital to fund the planned clinical trials;

inability to generate sufficient preclinical, toxicology, or other data to support the initiation of human clinical trials;

delays in reaching a consensus with regulatory agencies on trial design;



identifying, recruiting and training suitable clinical investigators;

delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

delays in obtaining required IRB approval at each clinical trial site;

delays in recruiting suitable patients to participate in our clinical trials;

delays due to changing standard of care for the diseases we are targeting;

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adding new clinical trial sites;

imposition of a clinical hold by regulatory agencies, after review of an IND application or equivalent application or an inspection of our clinical trial operations or trial sites;

failure by our CROs, other third parties or us to adhere to clinical trial requirements;

loss of product due to shipping delays or delays in customs in connection with delivery to foreign countries for use in clinical trials;

failure to perform in accordance with the FDA's good clinical practices, or GCP requirements or applicable regulatory guidelines in other countries;

inability to manufacture, test, release, import or export for use sufficient quantities of our product candidates for use in clinical trials;

failure to manufacture our product candidate in accordance with the FDA's good manufacturing practice, or GMP, requirements or applicable regulatory guidelines in other countries;

delays in the testing, validation and delivery of our product candidates to the clinical trial sites;

delays in having patients complete participation in a trial or return for post-treatment follow-up;

clinical trial sites deviating from trial protocol or clinical trial sites or patients dropping out of a trial;

occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;

changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;

the costs of clinical trials of our product candidates may be greater than we anticipate; or

clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon drug development programs.

Further, a clinical trial may be suspended or terminated by us, our collaborators, the IRBs, in the institutions in which such trials are being conducted, the Data Safety Monitoring Board, or DSMB, for such trial, or by the FDA or other regulatory authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience termination of, or delays in the completion of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. Furthermore, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

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Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. In addition, if we or our third-party collaborators make manufacturing or formulation changes to product candidates, we or they may need to conduct additional trial to bridge the modified product candidates to earlier versions. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

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If the results of our clinical trials are inconclusive or if there are safety concerns or adverse events associated with our product candidates, we may:

be delayed in obtaining marketing approval for our product candidates, if 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 or distribution restrictions or safety warnings;

be subject to changes with the way the product is administered;

be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;

have regulatory authorities withdraw their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy;

be subject to the addition of labeling statements, such as warnings or contraindications;

be sued; or

experience damage to our reputation.

Any of these events could prevent us from achieving or maintaining market acceptance of our product candidates and impair our ability to commercialize our product candidates.

***Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following any potential marketing approval.***

As with many pharmaceutical and biological products, treatment with our product candidates may produce undesirable side effects or adverse reactions or events. These adverse events may occur despite our belief that our AAV vectors have an improved safety profile over prior such treatments.

Known adverse side effects that could occur with treatment with AAV vectors include an immunologic reaction to the capsid protein or gene at early timepoints after administration. In previous clinical trials involving AAV viral vectors for gene therapy, some subjects experienced serious adverse events, including the development of T-cell response due to immune response against the vector capsid proteins. If our vectors demonstrate a similar effect, or other adverse events, we may be required to halt or delay further clinical development of our product candidates. In addition, theoretical adverse side effects of AAV vectors include replication and spread of the virus to other parts of the body and insertional oncogenesis, which is the process whereby the insertion of a functional gene near a gene that is important in cell growth or division results in uncontrolled cell division, also known as cancer, which could potentially enhance the risk of malignant transformation. Potential procedure-related events, including inflammation or injury to the eye, are similar to those associated with standard ophthalmic intervention procedures. There is also the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material.

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If any such adverse events occur, our clinical trials could be suspended or terminated and the FDA, the EMA or other foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. The product-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial. If we elect or are required to delay, suspend or terminate any clinical trial of any of our product candidates, the commercial prospects of such product candidates will be harmed and our ability to generate product revenues from any of these product candidates will be delayed or eliminated. Any of these occurrences may harm our business, financial condition and prospects significantly.

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Additionally, if any of our product candidates receive marketing approval, the FDA could require us to adopt a Risk Evaluation and Mitigation Strategy, or REMS, to ensure that the benefits outweigh its risks, which may include, among other things, a medication guide outlining the risks of gene therapies for distribution to patients and a communication plan to health care practitioners. Furthermore, if we or others later identify undesirable side effects caused by our product candidate, a number of potentially significant negative consequences could result, including:

regulatory authorities may withdraw approvals of such product candidate;

regulatory authorities may require additional warnings on the label;

we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;

we may be required to change the way a product candidate is administered or conduct additional clinical trials;

we could be sued and held liable for harm caused to patients; and

our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our product candidates and could significantly harm our business, prospects, financial condition and results of operations.

***We may be unable to obtain orphan product designation or exclusivity for some of our product candidates. If our competitors are able to obtain orphan product exclusivity for their products that are the same as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.***

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, 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 diagnosed annually 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, or COMP, 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 Community. Additionally, designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biological product. Our product candidates for the treatment of LCA2, XLRS, ACHM (in the form caused by mutations in the CNGB3 gene) and AAT deficiency have been granted orphan drug designations by the FDA, but at this time we have neither requested nor obtained orphan drug designation for any of our other product candidates. Even if we request orphan drug designation for our other product candidates, there can be no assurances that the FDA will grant any of our product candidates such designation. Additionally, the designation by the FDA of any of our product candidates as an orphan drug does not guarantee that the FDA will accelerate regulatory review of or ultimately approve that product candidate.

Generally, if a product candidate with an orphan drug designation subsequently 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 EMA or the FDA from approving another marketing application for the same drug and indication for that time period, except in limited circumstances. The applicable period is seven years in the United States and 10 years in Europe. The European exclusivity period 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 lost if the FDA or EMA determines



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that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different drugs can be approved for the same condition. In the United States, even after an orphan drug is approved, the FDA can subsequently approve another drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

***Even if we complete the necessary clinical trials, we cannot predict when or if we will obtain regulatory approval to commercialize a product candidate or the approval may be for a more narrow indication than we expect.***

We cannot commercialize a product candidate until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates demonstrate safety and efficacy in clinical trials, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process. Regulatory agencies also may approve a product candidate for fewer or more limited indications than requested, may not approve the price we intend to charge for our product candidate, may impose significant limitations in the form of narrow indications, warnings, precautions or contra-indications with respect to conditions of use or may grant approval subject to the performance of costly post-marketing clinical trials. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

***Even if we obtain regulatory approval for a product candidate, our products will remain subject to regulatory scrutiny.***

Even if we obtain regulatory approval in a jurisdiction for our product candidates, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, and submission of safety and other post-market information. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product. For example, the holder of an approved BLA is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. FDA guidance advises that patients treated with some types of gene therapy undergo follow-up observations for potential adverse events for as long as 15 years. The holder of an approved BLA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with GMP requirements and adherence to commitments made in the BLA or foreign marketing application. If we or a regulatory agency discovers previously unknown problems with a product such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured or disagrees with the promotion, marketing or labeling of that product, a regulatory agency may impose restrictions relative to that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.



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If we fail to comply with applicable regulatory requirements following approval of any of our product candidates, a regulatory agency may:

issue a warning letter asserting that we are in violation of the law;

seek an injunction or impose civil or criminal penalties or monetary fines;

suspend or withdraw regulatory approval;

suspend any ongoing clinical trials;

refuse to approve a pending BLA or comparable foreign marketing application (or any supplements thereto) submitted by us or our strategic partners;

restrict the marketing or manufacturing of the product;

seize or detain product or otherwise require the withdrawal of product from the market;

refuse to permit the import or export of products; or

refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenues.

In addition, the FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

***Even if we obtain and maintain approval for our product candidates from the FDA, we may never obtain approval for our product candidates outside of the United States, which would limit our market opportunities and adversely affect our business.***

Approval of a product candidate in the United States by the FDA does not ensure approval of such product candidate by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Sales of our product candidates outside of the United States will be subject to foreign regulatory requirements governing clinical trials and marketing approval. Even if the FDA grants marketing approval for a product candidate, comparable regulatory authorities of foreign countries must also approve the manufacturing and marketing of the product candidates in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials. In many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for our products, if approved, is also subject to approval. We intend to submit a marketing authorization application to the EMA for approval in the EEA, but obtaining such approval is a lengthy and expensive process and the EMA has its own procedures for approval of product candidates.

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Even if a product candidate is approved, the FDA or the EMA, as the case may be, may limit the indications for which the product may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming clinical trials or reporting as conditions of approval. Regulatory authorities in countries outside of the United States and the EEA also have requirements for approval of product candidates with which we must comply prior to marketing in those countries. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our product candidates in certain countries.

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Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries and regulatory approval of a product candidate in one country does not ensure approval in any other country, while a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. Also, regulatory approval for any of our product candidates may be withdrawn. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business will be adversely affected.

### **Risks related to our reliance on third parties**

***We expect to rely on third parties to conduct aspects of our product manufacturing and protocol development, and these third parties may not perform satisfactorily.***

We do not expect to independently conduct all aspects of our vector production, product manufacturing, protocol development, and monitoring and management of our ongoing and planned preclinical and clinical programs. We currently rely, and expect to continue to rely, on third parties for the production of our clinical trial materials. In such cases, we expect to control only certain aspects of their activities.

Under certain circumstances, these third parties may be entitled to terminate their engagements with us. If we need to enter into alternative arrangements, it could delay our product development activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations and study and trial protocols. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study and trial plans and protocols, or if there are disagreements between us and these third parties, we will not be able to complete, or may be delayed in completing, the preclinical studies and clinical trials required to support future IND submissions and approval of our product candidates. In some such cases we may need to locate an appropriate replacement third-party relationship, which may not be readily available or on acceptable terms, which would cause additional delay with respect to the approval of our product candidates and would thereby have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;

reduced control as a result of using third-party manufacturers for all aspects of manufacturing activities;

termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us; and

disruptions to the operations of our third-party manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier.

Any of these events could lead to clinical trial delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize future product candidates. Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of product manufacture.

***We and our contract manufacturer are subject to significant regulatory oversight with respect to manufacturing our products. The manufacturing facilities on which we rely may not continue to meet regulatory requirements and may have limited capacity.***

All parties involved in the preparation of therapeutics for clinical trial or commercial sale, including our existing contract manufacturer for our product candidates, SAFC Pharma, are subject to extensive regulation.



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Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with GMP requirements. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of a BLA on a timely basis and must adhere to the FDA's GMP requirements enforced by the FDA through its facilities inspection program. Our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities do not pass a pre-approval plant inspection, FDA approval of the products will not be granted.

The regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our third-party manufacturers. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or our third-party manufacturers to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a manufacturing facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If we or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new product candidate, or revocation of a pre-existing approval. Such an occurrence may cause our business, financial condition and results of operations to be materially harmed.

Additionally, if supply from an approved manufacturer is interrupted, there could be a significant disruption in commercial supply of our products. We do not currently have a backup manufacturer of our product candidate supply for clinical trials or commercial sale. An alternative manufacturer would need to be qualified through a BLA supplement which could result in further delay. The regulatory agencies may also require additional trials if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

***We expect to rely on third parties to conduct, supervise and monitor our clinical trials, and if these third parties perform in an unsatisfactory manner, it may harm our business.***

We expect to rely on academic research institutions and other CROs along with clinical trial sites to ensure our clinical trials are conducted properly and on time. While we will have agreements governing their activities, we will have limited influence over their actual performance and will control only certain aspects of our CROs' activities. Nevertheless, we will be responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities.

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We and our CROs are required to comply with the FDA's and other regulatory authorities' GCP, GMP and good laboratory practice, or GLP, requirements for conducting, recording and reporting the results of our preclinical studies and clinical trials to assure that the data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. The FDA enforces these requirements through periodic inspections of study sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with applicable GCP requirements, the clinical data generated in our future clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving any marketing applications. Upon inspection, the FDA may determine that our clinical trials did not comply with GCP requirements, which may render the data generated in those trials unreliable. In addition, our future clinical trials will require a sufficient number of test subjects to evaluate the safety and effectiveness of our product candidates. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of patients, we may be required to repeat such clinical trials, which would delay the regulatory approval process.

Our CROs are not our employees, and, except for remedies available to us under our agreements with such CROs, we are therefore unable to directly monitor whether or not they devote sufficient time and resources to our clinical and nonclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

Switching or adding CROs involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, prospects, financial condition and results of operations.

We also expect to rely on other third parties to store and distribute our vectors and products for any clinical trials that we may conduct. Any performance failure on the part of our distributors could delay clinical development, regulatory review or marketing approval of our product candidates or commercialization of our products, if approved, producing additional losses and depriving us of potential product revenue.

***Collaborations with third parties may be important to our business. If these collaborations are not successful, our business could be adversely affected.***

We entered into a collaboration with Genzyme relating to a wet AMD product candidate, which subsequently was modified to take the form of a license to Genzyme. Under our modified relationship, Genzyme became responsible for all future clinical and commercial development of the licensed wet AMD product candidate. Genzyme recently informed us that it no longer intends to use our HSV-based manufacturing technology to produce the AAV vector being used for the wet AMD product. Our license agreement with Genzyme was further amended in December 2013 to reflect this fact. We do not currently expect to derive substantial revenue from our license arrangement with Genzyme, but an unsuccessful outcome in pending and future clinical trials for which Genzyme is responsible could be harmful to the public perception and prospects of our gene therapy platform. Our license relationship with Genzyme, and any future collaboration we enter into in the future, may pose a number of risks, including the following:

collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;

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collaborators may not perform their obligations as expected;

collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;

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;

product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;

a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of any such product candidate;

disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development of any product candidates, might cause delays or termination of the research, development or commercialization of such product candidates, might lead to additional responsibilities for us with respect to such product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;

collaborators may not properly maintain or defend our intellectual property rights 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 potential litigation;

collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and

collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

If our collaborations do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of our gene therapy platform and product candidates could be delayed and we may need additional resources to develop product candidates and gene therapy platform. All of the risks relating to product development, regulatory approval and commercialization described in this prospectus also apply to the activities of our therapeutic program collaborators, if any.

Our license to Genzyme contains a restriction on our engaging in activities that are the subject of that collaboration. However, as a result of the December 2013 amendment of our agreement with Genzyme, these restrictions no longer apply to the field of treatments for ocular neovascularization disorders, including AMD. In addition, under that collaboration agreement, Genzyme has options, which expire in 2015 and 2017, to license our manufacturing technology as it existed at the time of the license for specified genes implicated in diseases outside our current area of focus. These restrictions, and any similar restrictions contained in future collaborations, may have the effect of preventing us

from undertaking development and other efforts that may appear to be attractive to us.



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Additionally, subject to its contractual obligations to us, if one of our collaborators is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

We may in the future determine to collaborate with pharmaceutical and biotechnology companies for development and potential commercialization of our product candidates. These relationships or those like them may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. In addition, we could face significant competition in seeking appropriate collaborators and the negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration agreement 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. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our product candidates because our research and development pipeline may be insufficient, our product candidates may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our product candidates as having the requisite potential to demonstrate safety and efficacy. If we license product candidates, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture. We cannot be certain that, following a strategic transaction or license, we will achieve the revenues or specific net income that justifies such transaction.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our gene therapy platform and our business may be materially and adversely affected.

***Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.***

Because we rely on third parties to manufacture our viral vectors and our product candidates, and because we collaborate with various organizations and academic institutions on the advancement of our gene therapy platform, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our collaborators, advisors, employees and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. We also

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conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

### **Risks related to commercialization of our product candidates**

***If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any revenues.***

We currently have no sales and marketing organization and have no experience selling and marketing our product candidates. To successfully commercialize any products that may result from our development programs, we will need to develop these capabilities, either on our own or with others. The establishment and development of our own sales force or the establishment of a contract sales force to market any products we may develop will be expensive and time-consuming and could delay any product launch. Moreover, we cannot be certain that we will be able to successfully develop this capability. We may enter into collaborations with other entities to utilize their mature marketing and distribution capabilities, but we may be unable to enter into marketing agreements on favorable terms, if at all. If our future collaborators do not commit sufficient resources to commercialize our future products, if any, and we are unable to develop the necessary marketing capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations to recruit, hire, train and retain marketing and sales personnel. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

***We face intense competition and rapid technological change and the possibility that our competitors may develop therapies that are more advanced or effective than ours, which may adversely affect our financial condition and our ability to successfully commercialize our product candidates.***

The biotechnology and pharmaceutical industries are characterized by intense and rapidly changing competition to develop new technologies and proprietary products, and any product candidates that we successfully develop and commercialize will have to compete with existing therapies and new therapies that may become available in the future. While we believe that our proprietary technology estate and scientific expertise in the gene therapy field provide us with competitive advantages, we face potential competition from many different sources, including larger and better-funded pharmaceutical, specialty pharmaceutical and biotechnology companies, as well as from academic institutions and governmental agencies and public and private research institutions that may develop potentially competitive products or technologies.

Currently there are no approved products for any of our lead orphan ophthalmology indications of XLRS, ACHM and XLRP. We believe the key competitive factors that will affect the success of our product candidates, if approved, are likely to be their efficacy, safety, convenience of administration and delivery, price, the level of generic competition and the availability of reimbursement from government and other third-party payors.

We believe a number of companies are working on AAV-based gene therapy technology, including Genzyme and its parent company Sanofi S.A., BioMarin Pharmaceutical Inc., uniQure B.V., Celladon Corp., Audentes Therapeutics, GenSight Biologics, ReGenX Biosciences, LLC, or ReGenX, Avalanche Biotechnologies, Inc., Spark Therapeutics, LLC, or Spark, Voyager Therapeutics, Inc., Dimension Therapeutics, Inc. and Sangamo Biosciences, Inc. We believe that companies developing gene therapies in the field of orphan ophthalmology on which we are currently focused include Genzyme and Spark, whose programs are at the clinical stage, and GenSight, Neurotech Pharmaceuticals, Inc. and ReGenX, as well as two smaller, early-stage

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companies, RetroSense Therapeutics, LLC and Eos Neuroscience, Inc., all of whose programs we believe are in the pre-clinical stage. Other companies could also seek to enter this field.

Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of treatments and the commercialization of those treatments. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

***The insurance coverage and reimbursement status of newly-approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our product, if approved, could limit our ability to market those products and decrease our ability to generate revenue.***

We expect the cost of a single administration of gene therapy products such as those we are developing to be substantial, when and if they achieve regulatory approval. We expect that coverage and reimbursement by governmental and private payors will be essential for most patients to be able to afford these treatments. Accordingly, sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government authorities, private health coverage insurers and other third-party payors. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

a covered benefit under its health plan;

safe, effective and medically necessary;

appropriate for the specific patient;

cost-effective; and

neither experimental nor investigational.

Obtaining coverage and reimbursement approval for a product from governmental and private payors is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data for the use of our products. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. If coverage and reimbursement are not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

There is significant uncertainty related to third-party coverage and reimbursement of newly approved products. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered and reimbursed. The Medicare and Medicaid programs increasingly are used as models for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Currently, no gene therapy products have been approved for coverage and reimbursement by the Centers for Medicare & Medicaid Services, or CMS, the agency responsible for administering the Medicare program, and it is difficult to predict what CMS will decide with respect to coverage and reimbursement for fundamentally novel products such as ours, as there is no body of established practices and precedents for these new products. Moreover, reimbursement agencies in Europe may be more conservative than CMS. For example,



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a number of cancer drugs have been approved for reimbursement in the United States and have not been approved for reimbursement in certain European countries. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries has and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

### ***Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of our product candidates or adversely affect our ability to conduct our business or obtain regulatory approvals for our product candidates.***

Gene therapy remains a novel technology, with no gene therapy product approved to date in the United States and only one gene therapy product approved to date in Europe. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians specializing in the treatment of those diseases that our product candidates target prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments they are already familiar with and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. For example, trials using early versions of lentiviral vectors, which integrate with, and thereby alter, the host cell's DNA, have led to several well-publicized adverse events, including reported cases of leukemia. Although none of our current product candidates utilize lentiviral vectors, our product candidates use a viral delivery system. Adverse events in our clinical trials, even if not ultimately attributable to our product candidates, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates.

### ***Healthcare legislative reform measures may have a material adverse effect on our business and results of operations.***

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or PPACA, was passed, which substantially changes the way health care is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The PPACA, among other things, subjects biologic products to potential competition by

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lower-cost biosimilars, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, subjects additional drugs to lower pricing under the 340B drug pricing program by adding new entities to the program and establishes a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

In addition, other legislative changes have been proposed and adopted in the United States since the PPACA was enacted. On August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect on April 1, 2013. 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.

***The commercial success of any of our product candidates will depend upon its degree of market acceptance by physicians, patients, third-party payors and others in the medical community.***

Ethical, social and legal concerns about gene therapy and genetic research could result in additional regulations restricting or prohibiting the products and processes we may use. Even with the requisite approvals from the FDA in the United States and other government bodies internationally, the commercial success of our product candidates will depend in part on the medical community's, patients', and third-party payors' acceptance of gene therapy products in general, and our product candidates in particular, as medically necessary, cost-effective, and safe. Any product that we bring to the market may not gain market acceptance by physicians, patients, third-party payors and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

the efficacy and safety of such product candidates as demonstrated in clinical trials;

the potential and perceived advantages of product candidates over alternative treatments;

the clinical indications for which the product candidate is approved;

the safety of product candidates seen in a broader patient group, including its use outside the approved indications;

the prevalence and severity of any side effects;

product labeling or product insert requirements of the FDA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;

the cost of treatment relative to alternative treatments;

relative convenience and ease of administration;

the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;

the strength of marketing and distribution support;

the timing of market introduction of competitive products;

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publicity concerning our products or competing products and treatments; and

sufficient third-party insurance coverage and reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in preclinical studies and clinical trials, market acceptance of the product will not be fully known until after it is launched. Our efforts to educate the medical community and third-party payors on the benefits of the product candidates may require significant resources and may never be successful. Such efforts to educate the marketplace may require more resources than are required by the conventional technologies marketed by our competitors. If any of our product candidates is approved but fails to achieve market acceptance among physicians, patients, or health care payors, we will not be able to generate significant revenues from such product, which could have a material adverse effect on our business, prospects, financial condition and results of operations.

***If we obtain approval to commercialize our product candidates outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.***

If any of our product candidates are approved for commercialization, we may enter into agreements with third parties to market them on a worldwide basis or in more limited geographical regions. We expect that we will be subject to additional risks related to entering into international business relationships, including:

different regulatory requirements for approval of drugs and biologics in foreign countries;

the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market (with low or lower prices) rather than buying them locally;

challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;

unexpected changes in tariffs, trade barriers and regulatory requirements;

economic weakness, including inflation, or political instability in particular foreign economies and markets;

compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;

foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;

difficulties staffing and managing foreign operations;

workforce uncertainty in countries where labor unrest is more common than in the United States;

potential liability under the Foreign Corrupt Practices Act of 1977 or comparable foreign regulations;



production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and

business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

These and other risks associated with our international operations may materially adversely affect our ability to attain or maintain profitable operations.

*We may not be successful in our efforts to identify or discover additional product candidates.*

The success of our business depends primarily upon our ability to identify, develop and commercialize product candidates based on our gene therapy platform. Although certain of our product candidates are currently in clinical or preclinical development, we may fail to identify other potential product candidates for clinical development for a number of reasons. For example, our research methodology may be unsuccessful in

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identifying potential product candidates or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

If any of these events occur, we may be forced to abandon our development efforts with respect to a particular product candidate, which would have a material adverse effect on our business and could potentially cause us to cease operations. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

### **Risks related to our business operations**

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

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. We will be subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which will require, among other things, that we file with the Securities and Exchange Commission, or the SEC, annual, quarterly and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the NASDAQ Global 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 will need to devote a substantial amount of time to these compliance initiatives. In particular, we will or may be required to:

prepare and distribute periodic public reports in compliance with our obligations under the federal securities laws;

establish an investor relations function;

establish new internal policies, such as those relating to disclosure controls and procedures and insider trading;

expand the roles and duties of our board of directors, our board committees and management;

institute a more comprehensive financial reporting and disclosure compliance function;

hire additional financial and accounting personnel and other experienced accounting and finance staff with the expertise to address the complex accounting matters applicable to public companies; and

establish an internal audit function.

We may not be successful in complying with these obligations, and compliance with these obligations could be time-consuming and expensive. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors. The increased costs will decrease our net income or increase our consolidated net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products or services.

We are evaluating these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their

application in practice may evolve over time

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as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting.

***We have identified material weaknesses in our internal control over financial reporting, and if we are unable to achieve and maintain effective internal control over financial reporting, investors could lose confidence in our financial statements and our company which could have a material adverse effect on our business and our stock price.***

In the course of preparing the financial statements that are included in this prospectus, our management has determined that we have material weaknesses in our internal control over financial reporting, which relate to the design and operation of our closing and financial reporting processes and our accounting for debt, equity and convertible instruments. We have concluded that these material weaknesses in our internal control over financial reporting are due to the fact that we do not have the appropriate resources with the appropriate level of experience and technical expertise to oversee our closing and financial reporting processes and to address the accounting and financial reporting requirements related to our issuances of convertible notes, preferred stock warrants, stock options, preferred stock and preferred stock purchase rights.

In order to remediate these material weaknesses, we are taking the following actions:

we are actively seeking additional accounting and finance staff members, including a permanent chief financial officer to succeed our interim chief financial officer and a senior accounting officer with public company reporting experience, to augment our current staff and to improve the effectiveness of our closing and financial reporting processes; and

we are formalizing our accounting policies and internal controls documentation and strengthening supervisory reviews by our management.

If we fail to fully remediate these material weaknesses or fail to maintain effective internal controls in the future, it could result in a material misstatement of our financial statements that would not be prevented or detected on a timely basis, which could cause investors to lose confidence in our financial information or cause our stock price to decline. Our independent registered public accounting firm has not assessed the effectiveness of our internal control over financial reporting and, under the JOBS Act, will not be required to provide an attestation report on the effectiveness of our internal control over financial reporting so long as we qualify as an emerging growth company, which may increase the risk that weaknesses or deficiencies in our internal control over financial reporting go undetected.

***If we are unable to manage expected growth in the scale and complexity of our operations, our performance may suffer.***

If we are successful in executing our business strategy, we will need to expand our managerial, operational, financial and other systems and resources to manage our operations, continue our research and development activities, and, in the longer term, build a sales force and commercial infrastructure to support commercialization

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of any of our product candidates that are approved for sale. Future growth would impose significant added responsibilities on members of management. It is possible that our management, finance, development personnel, systems and facilities currently in place may not be adequate to support this future growth. Our need to effectively manage our operations, growth and products requires that we continue to develop more robust business processes and improve our systems and procedures in each of these areas and to attract and retain sufficient numbers of talented employees. We may be unable to successfully implement these tasks on a larger scale and, accordingly, may not achieve our research, development and growth goals.

### ***Our future success depends on our ability to retain key employees, consultants and advisors and to attract, retain and motivate qualified personnel.***

We are highly dependent on our executive officers, the loss of whose services may adversely impact the achievement of our objectives. Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled executives and scientific personnel in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, failure to succeed in preclinical studies or clinical trials may make it more challenging to recruit and retain qualified personnel. The inability to recruit or loss of the services of any executive, key employee, consultant or advisor may impede the progress of our research, development and commercialization objectives.

In order to induce valuable employees to remain at AGTC, in addition to salary and cash incentives, we have provided stock options that vest over time. The value to employees of stock options that vest over time may be significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies.

Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us. The loss of the services of any of our executive officers or other key employees and our inability to find suitable replacements could potentially harm our business, prospects, financial condition or results of operations. We do not maintain key man insurance policies on the lives of these individuals or any of our other employees. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level, and senior managers as well as junior, mid-level, and senior scientific and medical personnel.

Many of the other biotechnology and pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They may also provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high quality candidates than what we can offer. If we are unable to continue to attract and retain high quality personnel, the rate and success at which we can discover, develop and commercialize product candidates will be limited.

### ***Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities.***

We are exposed to the risk that our employees, CROs, principal investigators, consultants and commercial partners may engage in fraudulent conduct or other illegal activity or may fail to disclose unauthorized activities to us. Misconduct by these parties could include intentional, reckless and/or negligent failures to comply with:

the laws and regulations of the FDA and non-U.S. regulators, including those laws requiring the reporting of true, complete and accurate information to such regulatory bodies;

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manufacturing standards we have established;

healthcare fraud and abuse laws and regulations in the United States and similar foreign laws; or

laws requiring the accurate reporting of financial information or data or the disclosure of unauthorized activities to us.

In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or 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.

***We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.***

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations may be directly, or indirectly through our prescribers, customers and purchasers, subject to various federal and state fraud and abuse laws, including, without limitation, the federal Health Care Program Anti-Kickback Statute, the federal civil and criminal False Claims Acts and Physician Payments Sunshine Act and regulations. These laws may impact, among other things, our proposed sales, marketing and educational programs. In addition, we may be subject to patient privacy laws by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include, but are not limited to:

the federal Health Care Program Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind in return for, the purchase, recommendation, leasing or furnishing of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;

federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other government payers that are false or fraudulent;

the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit a person from knowingly and willfully executing a scheme or from making false or fraudulent statements to defraud any healthcare benefit program, regardless of the payor (e.g., public or private);

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, and as amended again by the final HIPAA omnibus rule, Modifications to the HIPAA Privacy, Security, Enforcement, and Breach Notification Rules Under HITECH and the Genetic Information Nondiscrimination Act; Other Modifications to HIPAA, published in January 2013, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, health care clearinghouses and health care providers;

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federal transparency laws, including the federal Physician Payment Sunshine Act that requires disclosure of payments and other transfers of value provided to physicians and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations;

the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the Affordable Care Act, and its implementing regulations, which may impact, among other things, reimbursement rates by federal health care programs and commercial insurers; and

state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government, or otherwise restrict certain payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts in certain circumstances, such as specific disease states.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. In addition, recent health care reform legislation has strengthened these laws. For example, the PPACA, among other things, amends the intent requirements of the federal Anti-Kickback Statute and the criminal statute governing healthcare fraud. A person or entity can now be found guilty of violating the Anti-Kickback Statute and the federal criminal healthcare fraud statute without actual knowledge of the statute or specific intent to violate it. In addition, the PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

***If the use of our product candidates harms patients, we could be subject to costly and damaging product liability claims.***

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. For example, we may be sued if any product candidate we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

impairment of our business reputation;

withdrawal of clinical trial participants;

initiation of investigations by regulators;

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costs due to related litigation;

distraction of management's attention from our primary business;

substantial monetary awards to trial participants, patients or other claimants;

loss of revenue;

exhaustion of any available insurance and our capital resources;

the inability to commercialize our product candidates; and

decreased demand for our product candidates, if approved for commercial sale.

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. While we believe our product liability insurance coverage is sufficient in light of our current clinical programs, the amount of the product liability coverage that we carry varies from time to time, depending on a number of factors, the most significant of which are the nature and scope of the clinical trials in which we are engaged and the number of patients being treated with our product candidates in these trials. The amount of our product liability coverage as of December 31, 2013 was \$10.0 million. This amount may increase or decrease in the future. We may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability and any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. If and when we obtain marketing approval for product candidates, we intend to expand our insurance coverage to include the commercial sale of our products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

***If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.***

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment, manufacture and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. Although we believe that our procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

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 or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. 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. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.



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***We rely on our relationship with a professional employer organization for our human relations function and as a co-employer of our personnel, and if that party failed to perform its responsibilities under that relationship, our relations with our employees could be damaged and we could incur liabilities that could have a material adverse effect on our business.***

All of our personnel, including our executive officers, are co-employees of AGTC and a professional employer organization, TriNet HR Corporation, or TriNet. Under the terms of our arrangement, TriNet is the formal employer of all of our personnel, and is responsible for administering all payroll, including tax withholding, and providing health insurance and other benefits for these individuals. We reimburse TriNet for these costs, and pay TriNet an administrative fee for its services. If TriNet fails to comply with applicable laws, or its obligations under this arrangement, our relationship with our employees could be damaged. We could, under certain circumstances, be held liable for a failure by TriNet to appropriately pay, or withhold and remit required taxes from payments to, our employees. In such a case, our potential liability could be significant and could have a material adverse effect on our business.

***We or the third parties upon whom we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.***

Substantially all of our operations are conducted from our headquarters located near Gainesville, Florida. Hurricanes or other natural disasters could severely disrupt our operations, damage our research facilities or destroy stored research materials that could be difficult to replace, and otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. In addition, despite the implementation of security measures, our internal computer systems and those of our current and any future CROs and other contractors and consultants and collaborators are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure or that otherwise disrupted our operations or the operations of our third-party contract manufacturer, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. For example, the loss of clinical trial data from our clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. If our security measures, disaster recovery and business continuity plans are not adequate in the event of such a breach, serious disaster or similar event, we could incur substantial expenses and the further development and commercialization of our product candidates could be delayed, which could have a material adverse effect on our business.

***Interruptions in the supply of product or inventory loss may adversely affect our operating results and financial condition.***

Our product candidates are manufactured using technically complex processes requiring specialized facilities, highly specific raw materials and other production constraints. The complexity of these processes, as well as strict company and government standards for the manufacture and storage of our products, subjects us to production risks. While product batches released for use in clinical trials or for commercialization undergo sample testing, some defects may only be identified following product release. In addition, process deviations or unanticipated effects of approved process changes may result in these intermediate products not complying with stability requirements or specifications. Most of our product candidates must be stored and transported at temperatures within a certain range. If these environmental conditions deviate, our product candidates' remaining shelf-lives could be impaired or their efficacy and safety could become adversely affected, making them no longer suitable for use. The occurrence or suspected occurrence of production and distribution difficulties can lead to lost inventories, and in some cases product recalls, with consequential reputational damage and the risk of product liability. The investigation and remediation of any identified problems can cause production delays, substantial expense, lost sales and delays of new product launches. Any interruption in the supply of finished products or the loss thereof could hinder our ability to timely distribute our products and satisfy customer

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demand. Any unforeseen failure in the storage of the product or loss in supply could delay our clinical trials and, if our product candidates are approved, result in a loss of our market share and negatively affect our revenues and operations.

*We may use our financial and human resources to pursue a particular research program or product candidate and fail to capitalize on programs or product candidates that may be more profitable or for which there is a greater likelihood of success.*

Because we have limited resources, we may forego or delay pursuit of opportunities with certain programs or product candidates or for indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for product candidates may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

*Our ability to use our net operating loss carryforwards may be subject to limitation.*

Under Section 382 of the Internal Revenue Code of 1986, as amended, substantial changes in our ownership may limit the amount of net operating loss carryforwards that could be utilized annually in the future to offset our taxable income. Specifically, this limitation may arise in the event of a cumulative change in ownership of our company of more than 50% within a three-year period. Any such annual limitation may significantly reduce the utilization of our net operating loss carryforwards before they expire. The closing of this offering, alone or together with transactions in our stock that have occurred in the past and may occur in the future, may trigger an ownership change pursuant to Section 382, which could limit the amount of net operating loss carryforwards that could be utilized annually in the future to offset our taxable income, if any. Any such limitation, whether as the result of this offering, sales of common stock by our existing stockholders or additional sales of common stock by us after this offering, could potentially result in increased tax liability in future years. We have not completed a study to assess whether an ownership change has occurred, or whether there have been multiple ownership changes since our inception, due to the significant costs and complexities associated with such study. However, we believe it is likely that transactions that have occurred in the past, alone or together with the closing of this offering and other transactions that may occur in the future, would trigger an ownership change pursuant to Section 382, which could limit the amount of net operating loss carryforwards that could be utilized annually in the future to offset our taxable income, if any.

### **Risks related to our intellectual property**

*If we are unable to obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained 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 impaired.*

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 patent applications in the United States and abroad related to our novel technologies and product candidates.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too

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late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

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 countries may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in issued patents that protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Moreover, we may be subject to a third-party preissuance submission of prior art to the United States Patent and Trademark Office, or become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. 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 license, develop or commercialize current or future product candidates.

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

In addition, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. 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 owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

***Third parties may initiate legal proceedings alleging claims of intellectual property infringement, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.***

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and *inter partes* reexamination proceedings before the

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United States Patent and Trademark Office and corresponding foreign patent offices. Numerous United States and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire.

Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our formulations, methods for manufacture or methods of use, including combination therapy, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

***We may not be successful in obtaining or maintaining necessary rights to gene therapy product components and processes for our development pipeline through acquisitions and in-licenses.***

Presently we have rights to the intellectual property to develop our gene therapy product candidates. Because our programs may involve additional product candidates that may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights. In addition, our product candidates may require specific formulations to work effectively and efficiently and these rights may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

For example, we sometimes collaborate with United States and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such right of first negotiation for intellectual property, we may be unable to negotiate a license within the specified time frame or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

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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 license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to required third-party intellectual property rights, our business, financial condition and prospects for growth could suffer.

*If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.*

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues and is complicated by the rapid pace of scientific discovery in our industry. We are a party to intellectual property license agreements with the University of Florida Research Foundation, an affiliate of the University of Florida, Johns Hopkins University and the UAB Research Foundation, an affiliate of The University of Alabama at Birmingham, each of which is important to our business, and we expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty and other obligations on us. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license.

We may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. It is possible that we may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current product candidates or future products, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties.

In many cases, patent prosecution of our licensed technology is controlled solely by the licensor. If our licensors fail to obtain and maintain patent or other protection for the proprietary intellectual property we license from them, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, and our competitors could market competing products using the intellectual property. In certain cases, we control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners. Disputes may arise regarding intellectual property subject to a licensing agreement, including:

the scope of rights granted under the license agreement and other interpretation-related issues;

the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;

the sublicensing of patent and other rights under our collaborative development relationships;

our diligence obligations under the license agreement and what activities satisfy those diligence obligations;

the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and

the priority of invention of patented technology.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.



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

Competitors may infringe our patents or other intellectual property or the patents or other intellectual property of our licensors. In response, we may be required to file infringement claims, which can be expensive and time-consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us, alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours or our licensors is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

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. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

***Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court.***

If we or one of our licensing partners initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the United States Patent and Trademark Office, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review, and equivalent proceedings in foreign jurisdictions. Such proceedings could result in the revocation of or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection on one or more of our product candidates. Such a loss of patent protection could have a material adverse impact on our business.

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***We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.***

We employ individuals who 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, consultants and independent 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 our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of our employee's former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

***We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.***

We may be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. While it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. We could be subject to ownership disputes arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

***Intellectual property litigation could cause us to spend substantial resources and 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 compromise our ability to compete in the marketplace.

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

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the United States Patent and Trademark Office and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We rely on our outside counsel to pay these fees due to non-U.S. patent agencies. The United States Patent and Trademark Office and various non-U.S. governmental patent agencies require compliance with a number of



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procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, 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 patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market and this circumstance could have a material adverse effect on our business.

### ***Changes in United States patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.***

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity, and therefore obtaining and enforcing biotechnology patents is costly, time-consuming and inherently uncertain.

Recent 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. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The United States Patent and Trademark Office recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

Moreover, recent United States Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the United States Congress, the federal courts, and the United States Patent and Trademark Office, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

### ***We have not yet sought FDA approval of names for any of our product candidates and failure to secure such approvals could adversely affect our business.***

Any name we propose to use with our product candidates in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

### ***We may not be able to protect our intellectual property rights throughout the world.***

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States,

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or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

### **Risks related to this offering and ownership of our common stock**

***There has been no public market for our common stock prior to this offering, and you may not be able to resell our shares at or above the price you paid, or at all.***

Prior to this offering, there has been no public market for our common stock. We intend to apply to list our common stock on the NASDAQ Global Market, but an active trading market for our common stock may never develop or be sustained following this offering. If an active trading market for our common stock does not develop after this offering, the market price and liquidity of our common stock will be materially and adversely affected. You may not be able to sell your shares quickly or at the market price if trading in our common shares is not active. The offering price for our common stock will be determined by negotiations between us and the underwriters and may bear no relationship to the market price for our common stock after this offering. An active trading market for our common stock may not develop and the market price of our common stock may decline below the offering price. Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic partnerships or acquire companies or products by using our shares of common stock as consideration.

***The market price for our common stock may be volatile, which could contribute to the loss of your investment.***

Fluctuations in the price of our common stock could contribute to the loss of all or part of your investment. Prior to this offering, there has not been a public market for our common stock. Accordingly, the initial public offering price for the shares of our common stock may not be indicative of the price that will prevail in the trading market, if any, that develops following this offering. If an active market for our common stock develops and continues, the trading price of our common stock following this offering is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. Any of the factors listed below could have a material adverse effect on your investment in our common stock and our common stock may trade at prices significantly below the initial public offering price. In such circumstances the trading price of our common stock may not recover and may experience a further decline.

Factors affecting the trading price of our common stock may include:

our failure to develop and commercialize our product candidates;

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actual or anticipated fluctuations in our quarterly financial results or the quarterly financial results of companies perceived to be similar to us;

changes in the market's expectations about our operating results;

adverse results or delays in preclinical studies or clinical trials;

our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;

adverse regulatory decisions, including failure to receive regulatory approval for any of our product candidates;

success of competitive products;

adverse developments concerning our collaborations and our manufacturers;

inability to obtain adequate product supply for any product candidate for clinical trials or commercial sale or inability to do so at acceptable prices;

the termination of a collaboration or the inability to establish additional collaborations;

unanticipated serious safety concerns related to the use of any of our product candidates;

our ability to effectively manage our growth;

the size and growth, if any, of the orphan ophthalmology and other targeted markets;

our operating results failing to meet the expectation of securities analysts or investors in a particular period or failure of securities analysts to publish reports about us or our business;

changes in financial estimates and recommendations by securities analysts concerning our company, the gene therapy market, or the biotechnology and pharmaceutical industries in general;

operating and stock price performance of other companies that investors deem comparable to us;

overall performance of the equity markets;

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announcements by us or our competitors of acquisitions, new product candidates or programs, significant contracts, commercial relationships or capital commitments;

our ability to successfully market our product candidates;

changes in laws and regulations affecting our business, including but not limited to clinical trial requirements for approvals;

disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our product candidates and gene therapy platform;

commencement of, or involvement in, litigation involving our company, our general industry, or both;

changes in our capital structure, such as future issuances of securities or the incurrence of additional debt;

the volume of shares of our common stock available for public sale;

additions or departures of key scientific or management personnel;

any major change in our board or management;

changes in accounting practices;

ineffectiveness of our internal control over financial reporting;

sales of substantial amounts of common stock by our directors, executive officers or significant stockholders or the perception that such sales could occur; and

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general economic and political conditions such as recessions, interest rates, fuel prices, international currency fluctuations and acts of war or terrorism.

Broad market and industry factors may materially harm the market price of our common stock irrespective of our operating performance. The stock market in general, and the NASDAQ Global Market and the market for biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of the particular companies affected. The trading prices and valuations of these stocks, and of ours, may not be predictable. A loss of investor confidence in the market for technology or software stocks or the stocks of other companies which investors perceive to be similar to us, the opportunities in the digital simulation market or the stock market in general, could depress our stock price regardless of our business, prospects, financial conditions or results of operations.

***If securities analysts do not publish research or reports about our business or if they downgrade our stock, the price of our common stock could decline.***

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us, our business, our markets and our competitors. We do not control these analysts. If securities analysts do not cover our common stock after the closing of this offering, the lack of research coverage may adversely affect the market price of our common stock. Furthermore, if one or more of the analysts who do cover us downgrade our stock or if those analysts issue other unfavorable commentary about us or our business, our stock price would likely decline. If one or more of these analysts cease coverage of us or fails to regularly publish reports on us, we could lose visibility in the market and interest in our stock could decrease, which in turn could cause our stock price or trading volume to decline and may also impair our ability to expand our business with existing customers and attract new customers.

***The concentration of our capital stock ownership with insiders upon the closing of this offering will likely limit your ability to influence corporate matters.***

We anticipate that our executive officers, employees, directors, current 5% or greater stockholders, and their respective affiliates will together beneficially own or control, in aggregate, approximately % of the shares of our outstanding common stock, after giving effect to the conversion of all outstanding preferred stock and assuming no exercise of outstanding options or warrants following the closing of this offering (assuming no exercise of the underwriters' over-allotment option). As a result, these executive officers, directors and principal stockholders, acting together, will have substantial influence over most matters that require approval by our stockholders, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets or any other significant corporate transaction. Corporate action might be taken even if other stockholders, including those who purchase shares in this offering, oppose such action. These stockholders may delay or prevent a change of control or otherwise discourage a potential acquirer from attempting to obtain control of our company, even if such change of control would benefit our other stockholders. This concentration of stock ownership may adversely affect investors' perception of our corporate governance or delay, prevent or cause a change in control of our company, any of which could adversely affect the market price of our common stock.

***We are an emerging growth company, and the reduced reporting requirements applicable to emerging growth companies may make our common stock less attractive to investors.***

We are an emerging growth company, as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company for up to five years, although circumstances could cause us to lose that status earlier, including if the market value of our common stock held by non-affiliates exceeds

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\$700.0 million as of any December 31 before that time or if we have total annual gross revenue of \$1.0 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following June 30 or, if we issue more than \$1.0 billion in non-convertible debt during any three-year period before that time, we would cease to be an emerging growth company immediately. Even after we no longer qualify as an emerging growth company, we may still qualify as a smaller reporting company which would allow us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. As a result, changes in rules of U.S. generally accepted accounting principles or their interpretation, the adoption of new guidance or the application of existing guidance to changes in our business could significantly affect our financial position and results of operations.

***Sales of a substantial number of shares of our common stock by our existing stockholders in the public market may cause our stock price to decline.***

Sales of our common stock in the public market after this offering, or the perception that these sales may occur, could cause the market price of our common stock to decline. Based on our shares of common stock outstanding as of December 31, 2013, upon the closing of this offering, we will have \_\_\_\_\_ shares of common stock outstanding, assuming no exercise of the underwriters' over-allotment option. Of these, only the \_\_\_\_\_ shares of our common stock sold in this offering, plus any shares sold upon exercise of the underwriters' over-allotment option, will be freely transferable without restriction or additional registration under the Securities Act of 1933, as amended, or the Securities Act. The remaining shares outstanding after this offering will be available for sale, upon the expiration of the 180-day lock-up period beginning from the date of this prospectus, if applicable, subject to volume and other restrictions as applicable under Rule 144 under the Securities Act. Any or all of these shares may be released prior to expiration of the lock-up period at the discretion of the lead underwriter for this offering. After the lock-up agreements expire, up to an additional \_\_\_\_\_ shares of common stock will be eligible for sale in the public market, \_\_\_\_\_ of which shares are held by directors, executive officers and other affiliates and will be subject to volume limitations under Rule 144 under the Securities Act, assuming an initial public offering price of \$ \_\_\_\_\_ per share (the midpoint of the price range set forth on the cover page of this prospectus). In addition, \_\_\_\_\_ shares of common stock that are either subject to outstanding options or reserved for future issuance under our employee benefit plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act. To the extent these shares are sold, or if it is perceived that they will be sold, into the market, the market price of our common stock could decline. See "Shares Eligible for Future Sale" for a more detailed description of the restrictions applicable to the sale of shares of our common stock after this offering.

***Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.***

We expect that significant additional capital may be needed in the future to continue our planned operations, including conducting clinical trials, commercialization efforts, expanded research and development activities and costs associated with operating a public company. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time

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to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights, preferences and privileges senior to the holders of our common stock, including shares of common stock sold in this offering.

***You will experience immediate and substantial dilution in the net tangible book value of the shares you purchase in this offering.***

If you purchase shares of our common stock in this offering, you will experience immediate and substantial dilution, as the initial public offering price of our common stock will be substantially greater than the net tangible book value per share of our common stock. Based on an initial offering price of \$      per share, which is the midpoint of the range on the cover page of this prospectus, if you purchase our common stock in this offering, you will suffer immediate and substantial dilution of approximately \$      per share. Further, investors purchasing common stock in this offering will contribute approximately      % of the total amount invested by stockholders since our inception, but will own only approximately      % of the shares of common stock outstanding after giving effect to this offering. If the underwriters exercise their over-allotment option, or if outstanding options and warrants to purchase our common stock are exercised, you will experience additional dilution. For a further description of the dilution that you will experience immediately after this offering, see the section entitled Dilution.

***Our board of directors and management will have broad discretion over the use of the proceeds we receive in this offering and might not apply the proceeds in ways that increase the value of your investment.***

Our board of directors and management will have broad discretion to use the net proceeds from this offering, including for any of the purposes described in the section entitled Use of Proceeds, and you will be relying on the judgment of our board of directors and management regarding the application of these proceeds. You will not have the opportunity to influence our decisions on how to use the proceeds, and we may not apply the net proceeds of this offering in ways that increase the value of your investment. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. While we have not allocated these estimated net proceeds for any specific purposes, we expect to use the net proceeds from this offering to develop our product candidates and for general corporate purposes, including working capital. We may also use a portion of the proceeds to repay outstanding indebtedness or in acquisitions of businesses, products and technologies that are complementary to our business. Although we have from time to time evaluated possible acquisitions, we currently have no commitments or agreements to make any material acquisition, and we may not make any acquisitions in the future. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

***We do not currently intend to pay dividends on our common stock and, consequently, your ability to achieve a return on your investment will depend on the appreciation in the price of our common stock.***

We have never declared or paid any cash dividends on our common stock. We currently intend to retain any future earnings to fund our future growth and do not expect to declare or pay any dividend on shares of our common stock in the foreseeable future. As a result, you may only receive a return on your investment in our common stock if the market price of our common stock appreciates and you sell your shares at a price above your cost. The price of our common stock may not appreciate in value or ever exceed the price that you paid for shares of our common stock in this offering.

***We could be subject to securities class action litigation.***

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology companies have

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experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

*Anti-takeover provisions in our amended and restated certificate of incorporation and amended and restated bylaws, as well as provisions in Delaware law, might discourage, delay or prevent a change of control of our company or changes in our management and, therefore, depress the trading price of our common stock.*

Our amended and restated certificate of incorporation, amended and restated bylaws and Delaware law contain provisions that could have the effect of rendering more difficult or discouraging an acquisition deemed undesirable by our board of directors, even if doing so would benefit our stockholders or remove our current management. Our corporate governance documents include provisions:

providing for three classes of directors with the term of office of one class expiring each year, commonly referred to as a staggered board;

authorizing blank check preferred stock, which could be issued with voting, liquidation, dividend and other rights superior to our common stock;

limiting the liability of, and providing indemnification to, our directors and officers;

eliminating the ability of our stockholders to call and bring business before special meetings and to take action by written consent in lieu of a meeting;

requiring advance notice of stockholder proposals for business to be conducted at meetings of our stockholders and for nominations of candidates for election to our board of directors;

controlling the procedures for the conduct and scheduling of board and stockholder meetings;

limiting the determination of the number of directors on our board and the filling of vacancies or newly created seats on the board to our board of directors then in office; and

providing that directors may be removed by stockholders only for cause.

These provisions, alone or together, could delay hostile takeovers and changes in control or changes in our management.

As a Delaware corporation, we are also subject to provisions of Delaware law, including Section 203 of the Delaware General Corporation Law, which prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

The existence of the foregoing provisions and anti-takeover measures could limit the price that investors might be willing to pay in the future for shares of our common stock. They could also deter potential acquirers of our company, thereby reducing the likelihood that you could receive a premium for your common stock in an acquisition.





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**CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS**

This prospectus contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Exchange Act. In some cases, you can identify these statements by forward-looking words such as may, could, should, would, intend, will, expect, anticipate, believe, estimate, continue, plan, potential predict, project or the negative of those words. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements. You should read these statements carefully because they discuss our future expectations, contain projections of our future results of operations or of our financial condition or state other forward-looking information. These forward-looking statements include, among other things, statements about:

the anticipated timing, costs and conduct of our planned clinical trials for our ACHM and XLRS product candidates;

the anticipated timing, costs and conduct of our planned preclinical studies of our XLRP product candidate;

our plans to explore potential applications of our gene therapy platform in other indications in orphan ophthalmology;

our expectations regarding the clinical effectiveness of our product candidates;

our beliefs regarding the scalability and commercial viability of our HAVE manufacturing method;

our commercialization, marketing and manufacturing capabilities and strategy;

our intellectual property position;

our competitive position;

our expectations related to the use of proceeds from this offering; and

our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

These forward-looking statements reflect our management's beliefs and views with respect to future events and are based on estimates and assumptions as of the date of this prospectus and are subject to risks and uncertainties. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus, particularly in the Risk Factors section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments that we may make.

You should read this prospectus, the documents that we reference in this prospectus and the documents that we have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.



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**USE OF PROCEEDS**

We estimate that the net proceeds from our issuance and sale of \_\_\_\_\_ shares of our common stock in this offering will be approximately \$ \_\_\_\_\_ million, assuming an initial public offering price of \$ \_\_\_\_\_ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their over-allotment option in full, we estimate that the net proceeds from this offering will be approximately \$ \_\_\_\_\_ million, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

A \$1.00 increase or decrease in the assumed initial public offering price of \$ \_\_\_\_\_ per share would increase or decrease the net proceeds from this offering by approximately \$ \_\_\_\_\_ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions.

Similarly, a one million share increase (decrease) in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) the net proceeds to us by \$ \_\_\_\_\_ million, assuming the assumed initial public offering price of \$ \_\_\_\_\_ per share (the midpoint of the price range set forth on the cover page of this prospectus) remains the same, and after deducting estimated underwriting discounts and commissions.

We expect to use the net proceeds from this offering, together with cash and cash equivalents on hand, to continue the clinical trials of our XLRS and ACHM product candidates beyond the Phase 1/2 stages (which we believe are already adequately funded), expand preclinical studies of our XLRP product candidate, and explore potential applications of our gene therapy platform in other indications in orphan ophthalmology.

Specifically, we intend to apply the net proceeds of this offering as follows:

approximately \$ \_\_\_\_\_ million to fund a Phase 1/2 clinical trial and, if that is successful, to initiate a pivotal Phase 3 trial of our XLRS product candidate;

approximately \$ \_\_\_\_\_ million to fund a Phase 1/2 clinical trial and, if that is successful, to initiate a pivotal Phase 3 trial of our ACHM product candidate;

approximately \$ \_\_\_\_\_ million to fund additional preclinical studies of our XLRP product candidate;

approximately \$ \_\_\_\_\_ million to explore, through early preclinical studies, potential applications of our gene therapy platform in other indications in orphan ophthalmology; and

the remainder for working capital and other general corporate purposes.

We may also use a portion of the net proceeds to in-license, acquire or invest in complementary businesses, technologies, products or assets, though we have no present plans to make any such acquisition or investment. Pending the use of the net proceeds from this offering, we intend to invest the net proceeds in short-term, interest-bearing, investment-grade securities, certificates of deposit or government securities.

Our expected use of net proceeds from this offering represents our current intentions based upon our present plans and business condition. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering or the amounts that we will actually spend on the uses set forth above. Due to the many variables inherent in the development of gene therapy products at this time, such as the timing of patient enrollment, the timing and results of preclinical animal studies and clinical trials and the timing of regulatory submissions and evolving regulatory requirements, the amount and timing of our actual expenditures will depend upon such variables and we cannot currently predict the stage of development we expect the net proceeds of this offering to achieve for our clinical studies and product candidates.

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As a result, we will have broad discretion over the use of the net proceeds from this offering, and investors will be relying on our judgment regarding the application of the net proceeds of this offering. In addition, we might decide to postpone or not pursue certain clinical trials or preclinical activities if the net proceeds from this offering and the other sources of cash are less than expected.

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**DIVIDEND POLICY**

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and future earnings, if any, to finance the growth and development of our business. We do not expect to pay any cash dividends on our common stock in the foreseeable future. Payment of future dividends, if any, will be at the discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements, restrictions contained in any future financing instruments, provisions of applicable law and other factors the board deems relevant. See Risk Factors Risks related to this offering and ownership of our common stock We do not currently intend to pay dividends on our common stock and, consequently, your ability to achieve a return on your investment will depend on the appreciation in the price of our common stock.

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**Table of Contents****CAPITALIZATION**

The following table sets forth our cash and cash equivalents and capitalization as of December 31, 2013 on:

An actual basis;

A pro forma basis, giving effect to the conversion of all of our preferred stock into 9,120,081 shares of common stock upon the closing of this offering, the reclassification of our Series B purchase right liability to additional paid-in capital and the conversion of all outstanding warrants exercisable for shares of Series A-1, Series A-1A and Series B-1 preferred stock into warrants exercisable for shares of common stock, resulting in the preferred stock warrant liability being reclassified to additional paid-in capital, each upon the closing of this offering; and

A pro forma as adjusted basis, giving additional effect to the sale of \_\_\_\_\_ shares of our common stock offered in this offering, assuming an initial public offering price of \$ \_\_\_\_\_ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us and the filing and effectiveness of a restated certificate of incorporation upon the closing of this offering.

The pro forma information below is illustrative only and our capitalization following the closing of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read the following table in conjunction with our financial statements and related notes, Selected Financial Data and Management's Discussion and Analysis of Financial Condition and Results of Operations appearing elsewhere in this prospectus.

		As of December 31, 2013	
	Actual	Pro Forma (in thousands, except share and per share data)	Pro Forma as Adjusted
Cash and cash equivalents	\$ 8,998	\$ 8,998	\$
Short-term investments	\$ 19,000	\$ 19,000	\$
Convertible preferred stock and stockholders' equity:			
Convertible preferred stock, \$0.001 par value; Series A-1 to B-3; shares issued and outstanding: 222,843,265 actual; none pro forma or pro forma as adjusted	73,721		
Common stock, \$0.001 par value; 410,000,000 shares authorized; shares issued: 109,039 actual; 9,229,120 pro forma; _____ pro forma as adjusted		9	
Additional paid-in capital	12,354	86,281	
Accumulated deficit	(56,225)	(56,225)	
Total stockholders' (deficit) equity	\$ (43,871)	\$ 30,065	\$
Total capitalization	\$ (43,871)	\$ 30,065	\$

A \$1.00 increase (decrease) in the assumed initial public offering price of \$ \_\_\_\_\_ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents and total stockholders' (deficit) equity by approximately \$ \_\_\_\_\_ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses

payable by us. Similarly, a one million share increase (decrease) in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) each of cash and



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cash equivalents and total stockholders' equity (deficit) and total capitalization by \$       million, assuming the assumed initial public offering price of \$       per share (the midpoint of the price range set forth on the cover page of this prospectus) remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

**Table of Contents****DILUTION**

If you invest in our common stock, your interest will be diluted immediately to the extent of the difference between the initial public offering price per share you will pay in this offering and the pro forma as adjusted net tangible book value (deficit) per share of our common stock after this offering.

Our pro forma historical net tangible book value (deficit) as of December 31, 2013 was \$28.2 million, or \$3.06 per share of common stock, taking into account the expected conversion of all shares of our preferred stock outstanding as of that date into 9,120,081 shares of common stock and the conversion of all outstanding warrants exercisable for shares of Series A-1, Series A-1A and Series B-1 preferred stock into warrants exercisable for shares of common stock, resulting in the preferred stock warrant liability being reclassified to additional paid-in capital, each upon closing of this offering. Without giving effect to the conversion of our outstanding preferred stock into common stock and the conversion of our outstanding warrants exercisable for preferred stock into warrants exercisable for common stock, we had a historical net tangible book value (deficit) of \$(47.2) million, or \$(433.09) per share of common stock, as of December 31, 2013. Historical net tangible book value per share is equal to our total tangible assets, less total liabilities and preferred stock, divided by the number of outstanding shares of our common stock.

After giving effect to our issuance and sale of \_\_\_\_\_ shares of common stock in this offering at an assumed initial public offering price of \$ \_\_\_\_\_ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, the pro forma as adjusted net tangible book value (deficit) as of December 31, 2013 would have been \$ \_\_\_\_\_ million, or \$ \_\_\_\_\_ per share. This represents an immediate increase in pro forma net tangible book value to existing stockholders of \$ \_\_\_\_\_ per share. The initial public offering price per share will significantly exceed the pro forma as adjusted net tangible book value per share. Accordingly, new investors who purchase shares of common stock in this offering will suffer an immediate dilution of their investment of \$ \_\_\_\_\_ per share. The following table illustrates this per share dilution to the new investors purchasing shares of common stock in this offering without giving effect to the over-allotment option granted to the underwriters:

Assumed initial public offering price		\$
Historical net tangible book value (deficit) per share	\$ (433.09)	
Increase per share attributable to conversion of outstanding preferred stock and preferred stock warrants	\$ 436.15	
Pro forma historical net tangible book value (deficit) per share as of December 31, 2013	\$ 3.06	
Increase per share attributable to sale of shares of common stock in this offering	\$	
Pro forma as adjusted historical net tangible book value per share		\$
Dilution per share to new investors		\$

Each \$1.00 increase or decrease in the assumed initial public offering price of \$ \_\_\_\_\_ per share would increase or decrease the pro forma net tangible book value (deficit) by \$ \_\_\_\_\_ million, the pro forma net tangible book value (deficit) per share after this offering by \$ \_\_\_\_\_ per share and the dilution in pro forma net tangible book value (deficit) per share to investors in this offering by \$ \_\_\_\_\_ per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discount and offering expenses payable by us.

Similarly, a one million share increase (decrease) in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted net tangible book value per share after this offering by approximately \$ \_\_\_\_\_ and decrease (increase) the dilution per share to investors participating in this offering by approximately \$ \_\_\_\_\_, assuming the assumed initial public offering price of \$ \_\_\_\_\_ per share remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

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If the underwriters exercise their over-allotment option in full, the pro forma as adjusted net tangible book value (deficit) will increase to \$ \_\_\_\_\_ per share, representing an immediate increase to existing stockholders of \$ \_\_\_\_\_ per share and an immediate dilution of \$ \_\_\_\_\_ per share to new investors. If any shares are issued upon exercise of outstanding options or warrants, you will experience further dilution.

The following table summarizes, on a pro forma as adjusted basis as of December 31, 2013, after giving effect to the conversion of all of our outstanding preferred stock into common stock, the differences between the number of shares of common stock purchased from us, the total consideration paid to us and the average price per share paid by existing stockholders and by new investors purchasing shares of common stock in this offering. The calculation below is based on an assumed initial public offering price of \$ \_\_\_\_\_ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, before the deduction of the estimated underwriting discounts and commissions and estimated offering expenses payable by us:

	Shares Purchased		Total Consideration		Average
	Number	%	Amount	%	Price Per Share
Existing stockholders		%	\$	%	\$
New investors					\$
<b>Total</b>		100%	\$	%	\$

The number of shares purchased from us by existing stockholders is based on 9,229,120 shares of our common stock outstanding as of December 31, 2013, which gives effect to the conversion of all outstanding shares of our preferred stock into 9,120,081 shares of common stock upon the closing of this offering, and excludes:

59,247 shares of common stock issuable upon the exercise of preferred stock warrants outstanding and exercisable as of December 31, 2013, at a weighted average exercise price of \$13.64 per share;

782,965 shares of common stock issuable upon the exercise of stock options outstanding under our 2001 Stock Option Plan and our 2011 Stock Incentive Plan as of December 31, 2013, at a weighted average exercise price of \$3.23 per share;

185,140 shares of common stock available for future issuance under our 2001 Stock Option Plan and our 2011 Stock Incentive Plan as of December 31, 2013; and

an additional 1,279,999 shares of our common stock that will be made available for future issuance under our equity compensation plans upon the closing of this offering.

If the underwriters exercise their option to purchase additional shares from us in full, the number of shares held by new investors will increase to \_\_\_\_\_, or \_\_\_\_\_% of the total number of shares of common stock outstanding after this offering and the percentage of shares held by existing stockholders will decrease to \_\_\_\_\_% of the total shares outstanding.

**Table of Contents****SELECTED FINANCIAL DATA**

The following selected financial data should be read together with our financial statements and accompanying notes and Management's Discussion and Analysis of Financial Condition and Results of Operations appearing elsewhere in this prospectus. Our selected statement of operations data for the fiscal years ended June 30, 2012 and 2013 and our selected balance sheet data as of June 30, 2012 and 2013 are derived from our audited financial statements included elsewhere in this prospectus. Our selected statement of operations data for the six months ended December 31, 2012 and 2013 and our selected balance sheet data as of December 31, 2013 have been derived from our unaudited financial statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of results to be expected for any future period, and our interim results are not necessarily indicative of our results for the entire year or any future period. The selected financial data in this section are not intended to replace our financial statements and the related notes.

	Fiscal Year Ended June 30,		Six Months Ended December 31,	
	2012	2013	2012	2013
	(in thousands except per share data)			
<b>Statement of Operations Data:</b>				
Revenue:				
Grant revenue	\$ 718	\$ 439	\$ 293	\$ 466
Sponsored research revenue	364	503	156	307
<b>Total revenue</b>	<b>1,082</b>	<b>942</b>	<b>449</b>	<b>773</b>
Operating expenses:				
Research and development	2,354	3,133	1,156	3,673
General and administrative	787	1,403	649	1,971
<b>Total operating expenses</b>	<b>3,141</b>	<b>4,536</b>	<b>1,805</b>	<b>5,644</b>
Loss from operations	(2,059)	(3,594)	(1,356)	(4,871)
Other income (expense):				
Interest income		10		15
Interest expense	(69)	(191)	(152)	
Fair value adjustments to warrant liabilities (1)	204	(8)	5	(105)
Fair value adjustments to Series B purchase rights (1)		(1,207)	(437)	(2,838)
<b>Total other income (expense), net</b>	<b>135</b>	<b>(1,396)</b>	<b>(584)</b>	<b>(2,928)</b>
<b>Net loss</b>	<b>\$ (1,924)</b>	<b>\$ (4,990)</b>	<b>\$ (1,940)</b>	<b>\$ (7,799)</b>
Net loss per share, basic and diluted (2)	\$ (17.65)	\$ (45.78)	\$ (17.80)	\$ (71.55)
Weighted-average shares outstanding, basic and diluted (2)	109	109	109	109
Pro forma net loss per share, basic and diluted (unaudited) (2)		\$ (1.20)		\$ (1.13)
Weighted-average pro forma shares outstanding, basic and diluted (unaudited) (2)		4,146		6,885
	As of June 30,		As of December 31,	
	2012	2013	2013	
	(in thousands)			
<b>Balance Sheet Data:</b>				
Cash and cash equivalents	\$ 774	\$ 8,893	\$ 8,988	
Short-term investments	\$ 14,000		\$ 19,000	
Working capital	\$ (399)	\$ 20,051	\$ 28,106	

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Total assets	\$ 2,824	\$ 25,490	\$ 31,709
Current liabilities	\$ 1,494	\$ 3,460	\$ 1,644
Total stockholders (deficit) equity	\$ (31,290)	\$ (36,183)	\$ (43,871)

- (1) See note 6 of the notes to financial statements appearing elsewhere in this prospectus for a description of the fair value adjustments to our warrant liabilities and Series B purchase rights.
- (2) See note 2 of the notes to financial statements appearing elsewhere in this prospectus for a description of the method used to calculate basic and diluted net loss per share and pro forma basic and diluted net loss per share.

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**MANAGEMENT'S DISCUSSION AND ANALYSIS**

**OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS**

*You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes appearing in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the Risk Factors section of this prospectus, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. See Cautionary Note Regarding Forward-Looking Statements.*

**Overview**

We are a clinical-stage biotechnology company that uses our proprietary gene therapy platform to develop products designed to transform the lives of patients with severe inherited orphan diseases in ophthalmology. Our lead product candidates, which are each in the preclinical stage, are treatments for X-linked retinoschisis, or XLRS, achromatopsia, or ACHM, and X-linked retinitis pigmentosa, or XLRP. These rare diseases of the eye are caused by mutations in single genes, significantly affect visual function and currently lack effective medical treatments. For our XLRS product candidate, we expect to file an IND and initiate Phase 1/2 clinical trials in the United States in late 2014 with initial clinical data expected in mid-2015. For our ACHM product candidate, we expect to file an IND and initiate Phase 1/2 clinical trials in the United States in early 2015, with clinical data expected in late 2015. We have also begun preclinical studies for our product candidate addressing XLRP, a disease characterized by progressive degeneration of the retina, leading to total blindness in adult men. In the longer term, we will seek opportunities to take advantage of the adaptability of our gene therapy platform to address a range of genetic diseases, both within and beyond our initial focus area of orphan ophthalmology.

Since our inception in 1999, we have devoted substantially all of our resources to our development efforts relating to our proof-of-concept programs in ophthalmology and alpha-1 antitrypsin deficiency, or AAT deficiency, an inherited orphan lung disease, including activities to manufacture product in compliance with good manufacturing practices, preparing to conduct and conducting clinical trials of our product candidates, providing general and administrative support for these operations and protecting our intellectual property. We do not have any products approved for sale and have not generated any revenue from product sales. We have funded our operations primarily through the private placement of preferred stock, common stock, convertible notes and warrants to purchase preferred stock. We have also been awarded grant funding aggregating \$10.6 million since our inception, either independently or with our collaborators. Most recently, in May 2013, we and the University of Florida, or UF, were jointly awarded an \$8.3 million dollar grant from the National Eye Institute, or NEI, of the National Institutes of Health, or NIH, to support development of our ACHM product candidate. As a sub-awardee, we expect to receive \$3.9 million over five years under this grant.

We have incurred losses from operations in each year since inception. Our net losses were \$1.9 million and \$5.0 million for the fiscal years ended June 30, 2012 and 2013, respectively. Substantially all our net losses resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We expect our expenses will increase substantially in connection with our ongoing activities, as we:

conduct preclinical studies and clinical trials for our XLRS, ACHM and XLRP product candidates;

continue our research and development efforts, including exploration through early preclinical studies of potential applications of our gene therapy platform in other indications in orphan ophthalmology;

manufacture clinical trial materials and develop large-scale manufacturing capabilities;

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seek regulatory approval for our product candidates;

further develop our gene therapy platform;

add personnel to support our product development and commercialization efforts; and

operate as a public company.

We do not expect to generate revenue from product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our product candidates, which we expect will take a number of years and which we believe is subject to significant uncertainty. We expect that the net proceeds from this offering and our existing cash and cash equivalents will be sufficient to enable us to advance planned preclinical studies and clinical trials for our lead product candidates for at least the next 24 months. In order to complete the process of obtaining regulatory approval for our lead product candidates and to build the sales, marketing and distribution infrastructure that we believe will be necessary to commercialize our lead product candidates, if approved, we will require substantial additional funding. Also, our current operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop our products.

We expect to incur losses for the foreseeable future, and we expect these losses to increase as we continue our development of, and seek regulatory approvals for, our product candidates and begin to commercialize any approved products. Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Our ability to generate revenue from product sales will depend on a number of factors, including, among others, obtaining and maintaining adequate coverage and reimbursement from third-party payors for our product candidates and for gene therapy as a viable treatment option. Even if we are able to generate revenues from the sale of our products, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce our operations.

## **Financial operations overview**

### ***Revenue***

Our ability to generate product revenue and become profitable depends upon our ability to successfully commercialize products. To date, we have not generated any revenues from the sales of products. In the two fiscal years ended June 30, 2012 and 2013, all our revenues were derived from grants. Our grant revenue is primarily generated through research and development grant programs offered by federal, state, and local governments and agencies, including the United States Food and Drug Administration, or FDA, and by patient advocacy groups such as the Foundation Fighting Blindness, or FFB, and the Alpha-1 Foundation. Grant revenue is recognized when there is reasonable assurance that the grant will be received and we have complied with the terms of the grant. Prior to fiscal year 2012, we also derived revenue from collaboration and license fees received under our agreement with Genzyme Corporation, or Genzyme. We currently do not expect to derive substantial additional revenue from our agreement with Genzyme.

### ***Research and development expenses***

Research and development expenses consist primarily of costs incurred for the development of our product candidates, which include:

employee-related expenses, including salaries, benefits, travel and share-based compensation expense;

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expenses incurred under agreements with academic research centers, contract research organizations, or CROs, and investigative sites that conduct our clinical trials;

the cost of acquiring, developing, and manufacturing clinical trial materials; and

facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other supplies.

Research and development costs are expensed as incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites.

We cannot determine with certainty the duration and completion costs of the current or future clinical trials of our product candidates or if, when, or to what extent we will generate revenues from the commercialization and sale of any of our product candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any of our product candidates. The duration, costs, and timing of clinical trials and development of our product candidates will depend on a variety of factors, including:

the scope, rate of progress, and expense of our ongoing as well as any additional clinical trials and other research and development activities;

the countries in which trials are conducted;

future clinical trial results;

uncertainties in clinical trial enrollment rates or drop-out or discontinuation rates of patients;

potential additional safety monitoring or other studies requested by regulatory agencies;

significant and changing government regulation; and

the timing and receipt of any regulatory approvals.

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

From inception through June 30, 2013, we have incurred approximately \$46.4 million in research and development expenses. Our research and development expenses, categorized by product candidate or program, in fiscal years 2012 and 2013 were as follows:

Product candidate or program	Fiscal year ended	
	June 30,	
	2012	2013



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	(in thousands)	
XLRS	\$ 633	\$ 929
ACHM	151	685
XLRP		
LCA2	265	312
Other orphan ophthalmology indications		70
General research and process development	711	746
AAT deficiency	594	391
 Total	 \$ 2,354	 \$ 3,133

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We plan to increase our research and development expenses for the foreseeable future as we continue the development of our XLRs, ACHM and XLRP product candidates and explore potential applications of our gene therapy platform in other indications in orphan ophthalmology. Our current planned research and development activities include the following:

we expect to file an IND and initiate in late 2014 Phase 1/2 clinical trials in the United States to examine the feasibility, safety and efficacy of our XLRs product candidate;

we expect to file an IND and initiate in early 2015 Phase 1/2 clinical trials in the United States to examine the feasibility, safety and efficacy of our ACHM product candidate;

we are currently designing preclinical studies to further evaluate the ability of an AAV vector to delay disease progression in animal models of XLRP. If these studies are successful, we will conduct additional preclinical studies required for submission of an IND to the FDA; and

we will continue to manufacture clinical trial materials in support of our clinical trials.

### ***General and administrative expenses***

General and administrative expenses consist primarily of salaries and related costs for personnel, including share-based compensation and travel expenses for our employees in executive, operational, finance and human resource functions. Other general and administrative expenses include facility-related costs and professional fees for directors, accounting and legal services and expenses associated with obtaining and maintaining patents.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research and development and potential commercialization of our product candidates. We also anticipate increased expenses related to audit, legal, regulatory, and tax-related services associated with maintaining compliance with NASDAQ listing and Securities and Exchange Commission requirements, director and officer insurance premiums, and investor relations costs associated with being a public company. Additionally, if and when we believe a regulatory approval of the first product candidate appears likely, we anticipate an increase in payroll and related expenses as a result of our preparation for commercial operations, especially as it relates to the sales and marketing of our product candidates.

### ***Other income (expense), net***

Other income and expense consists primarily of interest earned on cash and cash equivalents and short-term investments, interest incurred on our bridge and bank loans, loss on disposal of property and equipment and re-measurement gain or loss associated with the change in the fair value of our Series B purchase rights liability and our preferred stock warrant liability.

We use the Black-Scholes option pricing model to estimate the fair value of our Series B purchase rights liability and preferred stock warrant liability. We base the estimates in the Black-Scholes option pricing model, in part, on subjective assumptions, including stock price volatility, risk-free interest rate, dividend yield, and the fair value of the preferred stock underlying the purchase rights and the warrants. The re-measurement gain or loss associated with the changes in the fair value of our Series B purchase rights liability and preferred stock warrant liability in each reporting period is recognized as a component of other income (expense), net.

### **Critical accounting policies and significant judgments and estimates**

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. 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



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to accrued expenses and share-based compensation. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be 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.

While our significant accounting policies are described in more detail in the notes to our financial statements appearing elsewhere in this prospectus, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our financial statements.

### ***Revenue recognition***

We have generated revenue primarily through sponsored research arrangements with nonprofit organizations for the development and commercialization of product candidates and revenues from federal research and development grant programs. We recognize revenue when amounts are realized or realizable and earned. Revenue is considered realizable and earned when the following criteria are met: (1) persuasive evidence of an arrangement exists; (2) delivery has occurred or services have been rendered; (3) the price is fixed or determinable; and (4) collection of the amounts due are reasonably assured.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue in our balance sheets. Amounts expected to be recognized as revenue within the twelve months following the balance sheet date are classified as current liabilities. We recognize revenue for reimbursements of research and development costs under collaboration agreements as the services are performed. We record these reimbursements as revenue and not as a reduction of research and development expenses, as we have the risks and rewards as the principal in the research and development activities.

We evaluate the terms of sponsored research agreement grants and federal grants to assess our obligations and if our obligations are satisfied by the passage of time, revenue is recognized on a straight-line basis. In situations where the performance of our obligations has been satisfied when the grant is received, revenue is recognized upon receipt of the grant. Certain grants contain refund provisions. We review those refund provisions to determine the likelihood of repayment. If the likelihood of repayment of the grant is determined to be remote, the grant is recognized as revenue. If the probability of repayment is determined to be more than remote, we record the grant as a deferred revenue liability, until such time that the grant requirements have been satisfied.

### ***Research and development costs and expenses***

Research and development costs are charged to expense as incurred. We recognize costs for certain development activities based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites. When outside contracts for research products or testing require advance payments, they are recorded on the balance sheet as a prepaid item and expensed when the service is provided or reaches a specific milestone outlined in the contract.

### ***Share-based compensation***

We account for our share-based compensation in accordance with ASC 718, *Compensation - Stock Compensation*. ASC 718 establishes accounting for share-based awards exchanged for employee services. Under the fair value recognition provisions of ASC 718, share-based compensation cost is measured at the grant date based on the fair value of the award and is recognized as expense over the requisite service/vesting period. Determining the appropriate fair value model and calculating the fair value of share-based payment awards require the use of highly subjective assumptions, including the expected life of the share-based payment awards and stock price volatility.

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We estimate the grant date fair value of stock options and the related compensation expense using the Black-Scholes option valuation model. This option valuation model requires the input of subjective assumptions including: (1) estimated period of time outstanding, or expected term, of the options granted, (2) volatility, (3) risk-free interest rate and (4) expected dividend yield. Because share-based compensation expense is based on awards ultimately expected to vest, it is reduced for estimated forfeitures. ASC 718 requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeiture rates differ from those estimates. We have estimated expected forfeitures of stock options based on our historical turnover rate and used these rates in developing a future forfeiture rate. If our actual forfeiture rate varies from our estimates, additional adjustments to compensation expense may be required in future periods. The assumptions used in calculating the fair value of share-based payment awards represent management's best estimates, but the estimates involve inherent uncertainties and the application of management judgment. As a result, if facts change and we use different assumptions, our share-based compensation expense could be materially different in the future.

*Exercise price and fair value of common stock*

All options have been granted at exercise prices determined by our board of directors to be not less than the fair value of the underlying shares on the date of grant. The fair value of the shares of common stock that underlie the stock options we have granted has historically been estimated by our board of directors based upon information available to it at the time of grant, as further discussed below.

Information pertaining to the Black-Scholes valuation of common stock options granted to employees during fiscal years 2012 and 2013 and the six months ended December 31, 2013 is as follows:

	Fiscal Year Ended June 30,		Six Months Ended December 31,	
	2012	2013	2012	2013
Options granted (number of shares)	3,934	193,066		371,718
Weighted-average exercise price	\$ 3.50	\$ 0.35	\$ 4.90	
Weighted-average grant date fair value of common stock options	\$ 1.75	\$ 0.35	\$ 4.90	
Assumptions:				
Expected volatility	65.02%	63.23%	60.00%	
Expected term in years	6.25	6.25	6.25	
Risk-free interest rate	1.39%	1.37% to 1.40%	2.05%	
Expected dividend yield	0.00%	0.00%	0.00%	

The dividend yield is based upon the assumption that we will not declare a dividend over the life of the options. Since adopting ASC 718, we have been unable to use historical employee exercise and option expiration data to estimate the expected term assumption for the Black-Scholes grant-date valuation. We have therefore utilized the simplified method, as prescribed by the SEC's Staff Accounting Bulletin No. 107, Share-Based Payment, to estimate on a formula basis the expected term of our stock options considered to have plain vanilla characteristics. The risk-free interest rate is based on the U.S. Treasury yield curve on the date of the grant. We compute volatility under the calculated value method of ASC 718 by utilizing the average of a peer group comprised of publicly-traded companies and expect to continue to do so until we have adequate historical data regarding the volatility of our traded stock price. The peer group was determined based upon companies considered to be direct competition or having been presented by independent parties as a comparable company based upon market sector. In determining a comparable, we have excluded large-cap entities. Forfeitures are estimated at the time of the grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Share-based compensation expense recognized in the statement of operations for the years ended June 30, 2012 and 2013 and the six months ended December 31, 2012 and 2013 does not record tax related effects on stock-based compensation given our historical and anticipated operating losses and offsetting changes in its valuation allowance that fully reserves against potential deferred tax assets.

**Table of Contents***Stock option grants during fiscal years 2012 and 2013*

The following table presents the grant dates, number of underlying shares and related exercise prices of all stock options granted to employees between July 1, 2011 and December 31, 2013, along with the fair value per share utilized to calculate share-based compensation expense for each grant:

<b>Date of grant</b>	<b>Number of shares</b>	<b>Exercise price per share</b>	<b>Common stock fair value per share on grant date</b>
August 25, 2011	3,999	\$ 3.50	\$ 3.50
November 2, 2011	3,934	3.50	3.50
January 6, 2013	192,067	0.35	0.35
April 19, 2013	999	0.35	0.35
September 18, 2013	371,718	4.90	4.90

Share-based compensation totaled \$24,445 and \$25,237 for fiscal years 2012 and 2013, and \$9,981 and \$111,247 for the six months ended December 31, 2012 and 2013, respectively. We expect the amount of our share-based compensation expense for stock options granted to employees and non-employees to increase in future periods due to increases in headcount and, potentially, to increases in the value of our common stock.

The intrinsic value of all vested and unvested options outstanding at December 31, 2013 was \$ , representing the difference between the aggregate value of the shares subject to such options, assuming a value per share equal to the midpoint of the price range on the cover page of this prospectus, and the aggregate exercise price of the such options, which have a weighted average exercise price equal to \$3.23 per share.

*Significant factors used in determining the fair value of our common stock*

The fair value of the shares of common stock that underlie the stock options we have granted has historically been determined by our board of directors based upon information available to it at the time of grant. The board of directors considered numerous objective and subjective factors in the assessment of fair value, including reviews of our business and financial condition, the conditions of the industry in which we operate and the markets that we serve and general economic, market and United States and global capital market conditions, the lack of marketability of our common stock, the likelihood of achieving a liquidity event for the shares of common stock underlying these stock options, the preferences and privileges of the preferred stock over the rights of the common stock, the status of the clinical trials and preclinical studies relating to our product candidates and third-party valuations of our common stock. The board has generally considered the most persuasive evidence of fair value to be the prices at which our securities were sold in actual arms length transactions.

*Background: awards prior to fiscal year 2012*

On six occasions in fiscal years 2004 through 2010, we issued shares of our preferred stock to venture capital investors. Our most recent preferred stock financing before fiscal year 2012 was on February 23, 2010, at which time we issued shares of our Series A-1 preferred stock for \$0.9658 per share (or \$33.80 per share on an as-converted to common stock basis). On November 4, 2010, we issued stock options for 28 shares of our common stock at an exercise price equal to \$3.50 per share, or approximately 10% of the as-converted purchase price of the Series A-1 preferred stock issued in February 2010, which our board determined to be not less than the fair value of our common stock. These were our last option grants prior to fiscal year 2012.

In estimating the fair value of our common stock as of November 4, 2010 and determining that this 10-to-1 ratio between the arms length price paid for our Series A-1 preferred stock and the estimated fair value of our common stock was reasonable, we took into account the early status of the clinical and preclinical studies relating to our product candidates, the lack of marketability of our common stock, the preferences and privileges of the preferred stock over the rights of the common stock, the lack of voting control on the part of the holders of

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the common stock and our assessment that there was a low likelihood of achieving a liquidity event that would result in the receipt of value by the holders of common stock underlying the stock options in the near term.

We also considered a retrospective third-party valuation of our common stock, dated as of June 30, 2010. In conducting its valuation, the valuation firm determined that the market approach was appropriate for a valuation of our equity, given the then-current stage of our development and the nature of our company. In applying the market approach, the valuation firm estimated our enterprise value on a marketable, control basis, based upon the \$0.9658 per share price paid for the Series A-1 preferred stock that we issued on February 23, 2010. After subtracting the liquidation preferences of our preferred stock, the valuation firm determined the equity value attributable to our common stock and, after applying a marketability discount of 40% and a control discount of 20%, concluded that the fair value of our common stock as of June 30, 2010 was \$3.50 per share.

### *Stock option grants on August 25, 2011*

In the first option award in fiscal year 2012, on August 25, 2011, our board awarded options for 3,999 shares of common stock at an exercise price of \$3.50 per share, which it determined to be not less than the fair value of our common stock.

In estimating the fair value of our common stock as of August 25, 2011, we took into account the lack of marketability of our common stock, the preferences and privileges of the preferred stock over the rights of the common stock, the lack of voting control on the part of the holders of the common stock and our assessment that there was a low likelihood of achieving a liquidity event for the shares of common stock underlying the stock options in the near term. We also considered developments in the preclinical and clinical trials of our product candidates, including the fact that we had been awarded a \$1.5 million grant from the Foundation Fighting Blindness to fund animal studies on our XLR5 program, which was a positive development, but also noted that we had not yet received data from the pending clinical trial of our most advanced proof-of-concept product candidate for the treatment of AAT deficiency.

We also considered a retrospective third-party valuation of our common stock, dated as of June 30, 2011. In conducting its valuation, the valuation firm determined that the market approach was appropriate for a valuation of our equity, given the then-current stage of our development and the nature of our company. In applying the market approach, the valuation firm estimated our enterprise value on a marketable, control basis, based upon the most recent arms length transaction, namely the \$0.9658 per share price paid for the Series A-1 preferred stock that we issued on February 23, 2010. After subtracting the liquidation preferences of our preferred stock, the valuation firm determined the equity value attributable to our common stock and, after applying a marketability discount of 40% and a control discount of 20%, concluded that the fair value of our common stock as of June 30, 2010 was \$3.50 per share.

Balancing these factors, we considered that there was no reason to increase or decrease our estimate of the fair value of our common stock from the previous estimate of \$3.50 per share.

### *Stock option grants on November 2, 2011*

On November 2, 2011, our board awarded options for 3,934 shares of common stock at an exercise price of \$3.50 per share, which it determined to be not less than the fair value of our common stock.

In estimating the fair value of our common stock as of November 2, 2011, we primarily considered that in November we received data from the clinical trials of our AAT deficiency product candidate, which was our most advanced program. The data were encouraging, in that they provided evidence of safety, dose response and sustained expression. However, in these trials the protein expression did not reach therapeutic levels. As a result, we concluded that additional development and clinical trials would be necessary for this product, and that it would be advisable for us to seek a partner with whom to share the cost of this effort.

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Balancing these factors, we considered that there was no reason to increase or decrease our estimate of the fair value of our common stock from the previous estimate of \$3.50 per share.

### *Stock option grants on January 6, 2013*

On January 6, 2013, our board awarded options for 192,067 shares of common stock at an exercise price of \$0.35 per share, which it determined to be not less than the fair value of our common stock.

The principal factor influencing our estimate of the fair value of our common stock as of January 6, 2013 was the fact that in November 2012, we entered into definitive agreements with respect to a \$37.5 million Series B preferred stock financing and sold 66,147,709 shares of our Series B-1 preferred stock at a price of \$0.1297 per share (or \$4.54 on an as-converted to common stock basis). The Series B-1 investment, which was led by a new investor, reflected a valuation of our company that was 87% lower than that reflected in the most recent Series A-1 financing in 2010.

We believe that the primary factors that influenced this lower valuation were the failure of our AAT deficiency product candidate to achieve serum AAT expression levels of 11  $\mu$ M or more in its clinical trials; the fact that we had not identified a partner to help fund continued development of our AAT deficiency program; the fact that our next most advanced product candidate, for the treatment of LCA2, while generating encouraging clinical data, addressed a disease with a small population estimated at only 600 patients in the United States and Europe; the fact that the commercial terms on which we had licensed our wet AMD product candidate to Genzyme were such that we no longer expected to receive substantial revenue from the wet AMD program; and the fact that our lead ophthalmology programs in XLRS and ACHM were still in an early and uncertain preclinical stage of development.

In connection with our Series B preferred stock financing, we obtained a contemporaneous, independent third-party valuation of our common stock, as of November 30, 2012, from the same firm that had previously performed annual valuations of our common stock. In conducting its valuation, the valuation firm again determined that the market approach was appropriate for a valuation of our equity, given the then-current stage of our development and the nature of our company. In applying the market approach, the valuation firm estimated our enterprise value on a marketable, control basis, based upon the most recent arms length transaction, namely the \$0.1297 per share price paid for the Series B preferred stock that we issued in November 2012. After subtracting the liquidation preferences of our preferred stock, the valuation firm determined the equity value attributable to our common stock was zero.

In estimating the fair value of our common stock, we recognized, as did the independent valuation firm, that any sale or other exit scenario at a valuation less than the accumulated liquidation preference (other than an initial public offering that resulted in mandatory conversion to common stock of our outstanding preferred stock), would result in the receipt by common stockholders of no consideration. In January 2013, conditions in the United States economy remained uncertain and the investment climate for biotechnology companies in general was not favorable, with investment in biotech companies in the United States, Europe and Canada declining in 2012 compared to 2011. We also considered that our business development efforts had not identified any strategic partner or collaborator for our programs other than the wet AMD program licensed to Genzyme. The initial public offering market in the United States was weak, no gene therapy company had ever reached the public markets, and we did not consider an initial public offering by our company to be a realistic option in the foreseeable future. We therefore considered the likelihood of any near term exit scenario at a valuation that would result in receipt of consideration by our common stockholders to be extremely low.

However, our board also did not regard as reasonable the independent valuation firm's assignment of zero value to our common stock. After considering the preferences and privileges of the preferred stock over the rights of the common stock and other factors bearing upon the relative values of our preferred stock and our common stock, we determined that a reasonable estimate of the fair value of our common stock at January 6, 2013 was \$0.35 per share. This represented approximately 8% of the as-converted price of the Series B-1 preferred stock



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we issued in November 2012, generally consistent with the discount we applied in determining the fair value of our common stock in relation to our previous preferred stock issuances.

### *Stock option grants on April 19, 2013*

On April 19, 2013, our board of directors awarded options for 999 shares of common stock at an exercise price of \$0.35 per share, which it determined to be not less than the fair value of our common stock.

In estimating the fair value of our common stock on April 19, 2013, we considered the positive development that in March 2013 we received initial funding under a \$0.3 million grant from the Alpha-1 Foundation to support our clinical trials of our product candidate addressing AAT deficiency. In March 2013, we also obtained primate data demonstrating the ability to deliver our product candidate addressing XLR5 by intravitreal injection, satisfying a milestone that resulted in the funding of a second tranche of our Series B financing, at a price equal to \$0.1485 per share (or \$5.20 on an as-converted to common stock basis). However, after taking into account the uncertain investment climate for gene therapy companies and what we still considered to be the very low likelihood of any near term exit scenario at a valuation that would result in receipt of consideration by our common stockholders, we concluded that there was no reason to increase or decrease our estimate of the fair value of our common stock from our previous estimate of \$0.35 per share as of January 6, 2013.

### *Stock option grants on September 18, 2013*

On September 18, 2013, our board of directors authorized the grant of options for 371,718 shares of common stock at an exercise price of \$4.90 per share, which it determined to be not less than the fair value of our common stock on that date. Share-based compensation expense attributable to these awards is accounted for in our statement of operations for the six months ended December 31, 2013.

By the time of these September 18, 2013 awards, conditions in the securities markets and the prospects for our industry in general, and our company in particular, had changed dramatically. A growing body of clinical data providing evidence of efficacy and safety of gene therapy in a variety of diseases, improvements in vector design and manufacturing processes by us and others and the establishment of regulatory guidelines for the development and approval of gene therapy products had led to increased investment from the biopharmaceutical industry. In November 2012, the first gene therapy treatment to be approved by any regulatory authority in the Western world had been approved by the European Commission, and in July 2013 the developer of the product announced that it had entered into a collaboration to commercialize the product. We also regarded the recent preclinical data demonstrating the feasibility of intravitreal delivery of AAV vectors in primates to be an important confirmation of the potential of our gene therapy approach in ophthalmic disease.

Meanwhile, the number of IPOs completed in the United States in the second calendar quarter of 2013 almost doubled compared to the first calendar quarter of 2013. More relevant to us, beginning in the second calendar quarter of 2013 and particularly in the third and fourth calendar quarters of 2013, the volume of initial public offerings by biotechnology companies accelerated significantly. Even more importantly, for the first time, these included offerings by companies in the early stages of developing treatments in various disease areas, including one based on gene therapy. As a result of these developments, we believed that investors had developed significant interest in the area of gene therapy.

Further, in May 2013, we and the University of Florida were jointly awarded an \$8.3 million dollar grant from the NEI to support development of our ACHM product, of which we expect to receive approximately \$3.9 million over five years. During the summer of 2013, we continued to make progress to complete the design and construction of vectors for our ACHM product candidate and in August 2013, we commenced preclinical animal studies of that product. We also made a number of key hires, including that of our chief business officer in September 2013.

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At a board meeting in August 2013, our board of directors and management reviewed recent developments in the IPO market for early-stage gene therapy companies and for the first time began to consider conducting an underwritten public offering of our common stock. We began interviewing investment banks, and by early September 2013, we had selected underwriters for a proposed initial public offering. The organizational meeting for the offering contemplated by this prospectus occurred on September 12, 2013.

In connection with establishing the exercise price for the September 18, 2013 option awards and estimating the fair value of our common stock as of September 18, 2013, we obtained a contemporaneous third-party valuation by an independent valuation firm other than that which had previously performed valuations of our common stock. This valuation, dated as of September 18, 2013, was conducted in accordance with the framework of the American Institute of Certified Public Accountants' Technical Practice Aid, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, or the Practice Aid, utilizing the probability weighted expected return method, or PWERM.

Using the PWERM method, the value of an enterprise's common stock is estimated based upon an analysis of future values for the company assuming various possible future liquidity events. Share value is based upon the probability-weighted present value of expected future net cash flows, considering each of the possible future events, as well as the rights and preferences of each share class.

As part of this valuation, we considered various scenarios involving the consummation of an initial public offering and our remaining a private company. We utilized the following probability-weighted scenarios:

Scenario	Probability
IPO by first calendar quarter of 2014	40%
IPO by second calendar quarter 2014	10%
Remain private through late 2015	50%

In assigning probabilities to the two IPO scenarios and to the remain private scenario, we considered the uncertainties affecting the public securities markets and the risk that we would be unable to successfully complete an initial public offering. We also considered the fact that as a result of our Series B financing in November 2012 and committed grants, we believe we have funding sufficient to enable us to complete planned preclinical studies and Phase 1/2 clinical trials for our lead product candidates, and therefore do not need to raise capital to reach a value inflection point. We believed that these factors made it less likely that we would complete a public offering, particularly if market conditions were unfavorable, and more likely that we would remain independent as a private company.

We used the market approach, in addition to considering the preliminary valuation indications that we received from various investment banking groups, to estimate our future exit values in connection with an assumed initial public offering of our common stock occurring in the first quarter of 2014, or IPO scenario 1, and the second quarter of 2014, or IPO scenario 2. In making this estimate, we considered the current stage of development of our various product candidates, analysis of pre-money valuations in recent IPOs by other companies of similar size at similar stages of clinical development, the strength of the current market for initial public offerings in the biotechnology industry and the preliminary valuations provided to us by various investment banking groups with which we met in August 2013.

In considering the remain private scenario, we applied the option-pricing model, or OPM, back-solve method to solve for the equity value and corresponding value of common stock based on the \$5.20 price per share of common stock issuable upon the conversion of Series B-2 preferred stock sold in April 2013. The OPM pricing method treats preferred and common stock as call options on the enterprise's value, with exercise prices based on the liquidation and conversion preferences of the preferred stock, and based on the common equity per-share values equal to outstanding option and warrant exercise prices. The option pricing method relies on a number of inputs, including the expected time to a liquidity event, the risk free rate, volatility and expected dividend yield.

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We utilized the following assumptions as inputs in the option-pricing method:

<b>Assumption</b>	<b>Value</b>
Expected time to liquidity	2.25 years
Risk-free interest rate	0.36%
Volatility	60.0%
Expected dividend yield	0.0%

We assumed an expected time to a liquidity event of approximately 2.25 years, which equates to a liquidity event occurring at December 31, 2015. In arriving at this estimate, we considered our cash position and burn rate, the stage of clinical development of our product candidates and upcoming clinical milestones. We selected a risk free rate equal to the yield on the U.S. Treasury bond, stripped principal, with a maturity date approximating the expected liquidity date. Based on an expected liquidity date of December 31, 2015, we utilized a risk-free interest rate of 0.36%. We estimated volatility equal to 60.0%, which approximates the third quartile of the re-levered volatilities from a group of guideline companies that we considered similar to us in size and diversification. Because we have never declared a dividend on our common stock and do not expect to do so in the foreseeable future, we utilized an assumed 0.0% dividend yield.

After applying the probability weightings described above, we determined the probability-weighted marketable value of the common stock based on the three scenarios to equal \$6.30 per share on a marketable minority interest basis.

We then applied a discount for lack of marketability, or DLOM, of our common stock. We utilized the Black-Scholes standard put option model and the average-strike put option pricing model to estimate the DLOM. Based upon these methods, we considered an appropriate DLOM to be 20%. Taking this into account, we determined the fair value of our common stock to be \$4.90 per share as of September 18, 2013.

***Warrant liability***

As of June 30, 2012 and 2013 and December 31, 2013, we had warrants outstanding to purchase shares of our Series A-1, Series A-1A and Series B-1 preferred stock. Because our Series A-1, Series A-1A and Series B-1 preferred stock are subject to redemption under circumstances outside of our control, the outstanding shares of these series of preferred stock are presented as temporary equity. Consequently, the warrants to purchase shares of Series A-1, Series A-1A and Series B-1 preferred stock are accounted for as liabilities and adjusted to fair value at the end of each reporting period. The fair value of the warrants classified as liabilities is estimated using the Black-Scholes option pricing model. The estimates in Black-Scholes option pricing model are based, in part, on subjective assumptions, including stock price volatility, term of the warrants, risk free interest rate, dividend yield, and fair value of the preferred stock underlying the warrants. Such assumptions could differ materially in the future. The gain or loss associated with the change in the fair value of the preferred stock warrant liability from the prior period is recognized as a component of other (expense) income, net.

***Series B purchase rights***

In November 2012, we entered into a Series B-1, B-2 and B-3 Preferred Stock Purchase Agreement, or Series B Purchase Agreement, which authorized the sale of up to 290,781,972 shares of convertible preferred stock in three separate tranches of Series B-1, Series B-2 and Series B-3 preferred stock, respectively. Simultaneously with the execution of the Series B Purchase Agreement, we issued and sold an aggregate of 66,147,709 shares of Series B-1 preferred stock at a price per share of \$0.1297. The Series B Purchase Agreement provided that the holders of the Series B-1 shares, or Series B holders, were also entitled to purchase up to an aggregate of 140,542,178 shares of Series B-2 preferred stock for an aggregate purchase price equal to \$18.2 million, or second tranche, and up to an aggregate of 82,670,167 shares of Series B-3 preferred stock for an aggregate purchase price equal to \$10.7 million, or third tranche. The price per share and number of shares to be issued in exchange for such amount was to be determined separately for each tranche by reference to which, if any, of three milestones specified in the agreement had been satisfied by us.

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The purchase rights were legally separable and exercisable apart from the Series B-1 shares and, because representatives of the Series B holders hold a majority of the seats on the board of directors, the decision to complete the second and third tranche was deemed to be outside our control. We therefore recorded, at the time of entry into the Series B Purchase Agreement, a Series B purchase rights liability of \$1.7 million for the fair value of our obligation to sell the Series B-2 and Series B-3 preferred stock in the second and third tranche. The Series B purchase rights liability was valued separately for each series using the Black-Scholes option-pricing method to assign a value to the purchase right relating to that series under each of the possible applicable valuation scenarios, depending on which milestones were met, with each scenario being assigned an estimated probability as of the valuation date. The aggregate of these probability-weighted valuations was assigned as the value of the purchase right for each tranche. The initial fair value of the Series B purchase rights liability was estimated to be \$0.6 million for the second tranche and \$1.1 million for the third tranche. The total value allocated to the Series B purchase rights reduced the amount allocated to the carrying value of the Series B-1 preferred stock on our balance sheet.

The most significant and judgmental inputs driving the fair value of our Series B purchase rights are the assumptions regarding the fair value of the underlying preferred shares and the volatility factor. With all other inputs constant, an increase or decrease in the assumed fair value of the preferred shares would result in a higher or lower estimate of the fair value of the Series B purchase rights, respectively, although there would not be a direct correlation. Similarly, an increase or decrease in the assumed volatility factor would result in a higher or lower estimate of the fair value of the Series B purchase rights, respectively.

In April 2013, following the satisfaction by us of the first milestone, the Series B holders exercised their rights with respect to the second tranche and purchased an aggregate of 122,749,639 shares of Series B-2 preferred stock at a price per share of \$0.1485, for gross cash proceeds of \$18.2 million. During fiscal year 2013, we recorded a change in value of the Series B purchase rights liability of \$1.2 million to other expense and the \$0.8 million balance of the value allocated to the Series B-2 purchase rights liability immediately prior to the closing of the second tranche was recorded as proceeds from the issuance of the Series B-2 preferred stock.

In October 2013, the Series B holders exercised their rights with respect to the third tranche and on November 5, 2013, we sold to the Series B holders an aggregate of 58,816,897 shares of our Series B-3 preferred stock at a price per share of \$0.1823 (or \$6.38 on an as-converted to common stock basis), for gross cash proceeds of \$10.7 million. In connection with the closing of the third tranche, we and the Series B holders amended the terms of the Series B purchase agreement to provide that if the two remaining milestones specified in the Series B Purchase Agreement are not satisfied by September 2014, the Series B holders who continue to hold shares of Series B-3 preferred stock will be entitled to receive an aggregate of approximately 13.4 million additional shares of Series B-3 preferred stock. This right will be extinguished upon the conversion to common stock of all outstanding shares of our preferred stock upon the closing of this offering.

During the six months ended December 31, 2013, we recorded a change in value of the Series B purchase right liability of \$2.8 million to other expense, and \$4.9 million allocated to the Series B-3 purchase right immediately prior to the closing of the third tranche was reallocated to the carrying value of the Series B-3 preferred stock.

The significant assumptions used as inputs in the Black-Scholes valuation were as follows:

<b>Assumption</b>	<b>Year Ended June 30, 2013</b>	<b>Six Months Ended December 31, 2013</b>
Exercise price	\$0.1297 to \$0.1823	\$0.1485 to \$0.1823
Years to maturity	0.37 to 1.87	0.00 to 1.00
Risk-free interest rate	0.04% to 0.25%	0.06% to 0.10%
Volatility	40.0% to 60.0%	55% to 85.0%

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### ***Income taxes***

We recognize deferred taxes for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. At June 30, 2013, we had net operating losses of approximately \$46.9 million that may be applied against future taxable income and expire in various years from 2022 to 2033. At June 30, 2013, we also had research and development tax credits of approximately \$0.9 million that may provide future tax benefits and expire from 2027 to 2042.

We periodically evaluate the positive and negative evidence bearing upon the realizability of our deferred tax assets. Based on our history of operating losses, we have concluded that it is more likely than not that the benefit of our deferred tax assets will not be realized. Therefore, any tax benefits to be realized in future years as a result of the utilization of our net operating loss carry forwards as of June 30, 2013, computed based on statutory federal and state rates, are completely offset by valuation allowances.

Under Section 382 of the Internal Revenue Code of 1986, as amended, substantial changes in our ownership may limit the amount of net operating loss carryforwards that could be utilized annually in the future to offset our taxable income. Specifically, this limitation may arise in the event of a cumulative change in ownership of our company of more than 50% within a three-year period. Any such annual limitation may significantly reduce the utilization of our net operating loss carryforwards before they expire. We have not completed a study to assess whether an ownership change has occurred, or whether there have been multiple ownership changes since our inception, due to the significant costs and complexities associated with such study. However, we believe it is likely that transactions that have occurred in the past, alone or together with the closing of this offering and other transactions that may occur in the future, would trigger an ownership change pursuant to Section 382, which could limit the amount of net operating loss carryforwards that could be utilized annually in the future to offset our taxable income, if any.

For all years through June 30, 2013, we generated research credits but we have not conducted a study to document the qualified activities. When completed, this study may result in an adjustment to our research and development credit carry forwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position for these two years. A full valuation allowance has been provided against our research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the deferred tax asset established for the research and development credit carry forwards and the valuation allowance.

Our policy is to recognize interest and penalties related to uncertain tax positions in income tax expense. As of June 30, 2012 and 2013 and at December 31, 2013, we had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in our statements of operations.

### **Internal control over financial reporting**

Our management is responsible for establishing and maintaining adequate internal control over financial reporting for our company. Internal control over financial reporting is a process to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States. Internal control over financial reporting includes maintaining records that in reasonable detail accurately and fairly reflect our transactions; providing reasonable assurance that transactions are recorded as necessary for preparation of our financial statements; providing reasonable assurance that receipts and expenditures of our assets are made in accordance with management's authorization; and providing reasonable assurance that unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements would be prevented or detected on a timely basis. Because of its inherent limitations, internal control over financial reporting is not intended to provide absolute assurance that a misstatement of our financial statements would be prevented or detected. Furthermore, our controls and procedures can be circumvented by the individual acts of some persons, by collusion of two or more people or by management override of the control, and misstatements due to error or fraud may occur and not be detected on a timely basis.



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Total revenue	\$	1,082	\$	942	\$	(140)	(13)%
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Grant revenue decreased by \$0.3 million from \$0.7 million to \$0.4 million from fiscal year 2012 to fiscal year 2013. The decrease was primarily the result of the timing of the release of funding under our FDA orphan grants relating to our LCA2 and AAT deficiency product candidates. Sponsored research revenue increased by

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\$0.1 million from \$0.4 million to \$0.5 million from fiscal year 2012 to fiscal year 2013. The increase was primarily the result of increased activity under our sponsored research arrangement with FFB related to the development of our XLRS product candidate.

*Research and development expense*