Spark Therapeutics, Inc.
Form 10-Q
August 10, 2016
Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-Q

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

For the quarterly period ended June 30, 2016

OR

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

For the transition period from to

Commission File Number: 001-36819

Spark Therapeutics, Inc.
(Exact Name of Registrant as Specified in Its Charter)

Delaware	46-2654405
(State or Other Jurisdiction of Incorporation or Organization)	(IRS Employer Identification No.)
3737 Market Street Suite 1300 Philadelphia, PA	19104
(Address of Principal Executive Offices)	(Zip Code)

(888) 772-7560
(Registrant's Telephone Number, Including Area Code)

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No ¨
Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during

the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No ¨

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

Large accelerated filer ¨ Accelerated filer ¨

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

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

As of August 3, 2016 there were 30,621,155 shares of the registrant’s Common Stock, par value $0.001 per share, outstanding.

Table of Contents

TABLE OF CONTENTS

Table of Contents

REFERENCES TO SPARK

In this Quarterly Report on Form 10-Q, unless otherwise stated or the context otherwise requires:

- references to “Spark LLC” refer to Spark Therapeutics, LLC only (which was previously known as AAVenue Therapeutics, LLC);
- references to “Spark Inc.” refer to Spark Therapeutics, Inc. only;
- references to “Spark,” “we,” “us,” “our” and similar references refer to Spark Inc., together with Spark LLC;
- references to the “corporate conversion” refer to all of the transactions related to the conversion of Spark LLC into Spark Inc., including the conversion of all of the outstanding membership interests of Spark LLC into shares of capital stock of Spark Inc.;
- references to (i) common stock refer to the common stock of Spark Inc. or, as applicable, to the common units of Spark LLC and (ii) preferred stock refer to the preferred stock of Spark Inc. or, as applicable, to the preferred units of Spark LLC;
- references to “Spark’s clinical trials” and similar references regarding clinical trials relating to our product candidates and the associated data (including the use of “we,” “us” and “our”) include the applicable rights to clinical and preclinical programs assigned or licensed to us by the Children’s Hospital of Philadelphia, or CHOP, or the University of Iowa Research Foundation;
- references to “Spark’s intellectual property” and similar references regarding intellectual property relating to our product candidates (including the use of “we,” “us” and “our”) include the applicable rights to intellectual property assigned or licensed to us by CHOP, the University of Iowa Research Foundation or the University of Pennsylvania; and
- references to “Spark’s manufacturing platform” and similar references regarding manufacturing of gene therapy product candidates (including the use of “we,” “us” and “our”) include the applicable know-how assigned or licensed to us by CHOP.

PART I. FINANCIAL INFORMATION

Item 1. Financial Statements

Spark Therapeutics, Inc.
Consolidated balance sheets
(unaudited)

	December 31, 2015	June 30, 2016
Assets		
Current assets:		
Cash and cash equivalents	$293,530,590	$225,026,665
Marketable securities	—	107,185,716
Other receivables	16,944,568	1,233,355
Prepaid expenses and deferred financing costs	1,132,626	1,830,138
Total current assets	311,607,784	335,275,874
Marketable securities	—	46,839,587
Property and equipment, net	16,999,445	19,554,010
Acquired-in-process research and development	—	15,490,000
Goodwill	—	2,096,119
Other assets	1,165,285	1,078,917
Total assets	$329,772,514	$420,334,507
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$9,687,594	$6,764,933
Accrued expenses and other	6,529,263	5,922,804
Current portion of deferred rent	715,959	751,483
Current portion of deferred revenue	5,182,835	5,168,674
Total current liabilities	22,115,651	18,607,894
Long-term deferred rent	8,084,509	7,687,001
Long-term deferred revenue	9,034,559	6,471,463
Deferred tax liability	—	1,936,250
Total liabilities	39,234,719	34,702,608
Stockholders' equity:		
Preferred stock, $0.001 par value. Authorized, 5,000,000 shares; no shares issued or outstanding	—	—
Common stock, $0.001 par value. Authorized, 150,000,000 shares; issued 27,082,493 and 30,579,756 shares at December 31, 2015 and June 30, 2016, respectively; 27,073,287 and 30,570,550 outstanding at December 31, 2015 and June 30, 2016, respectively	27,083	30,580
Additional paid-in capital	419,791,732	569,061,035
Accumulated other comprehensive income	—	74,130
Treasury stock, at cost 9,206 shares at December 31, 2015 and June 30, 2016	(552,636)	(552,636)
Accumulated deficit	(128,728,384)	(182,981,210)
Total stockholders' equity	290,537,795	385,631,899
Total liabilities and stockholders' equity	$329,772,514	$420,334,507

See accompanying notes to the unaudited consolidated financial statements.

2

Spark Therapeutics, Inc.
Consolidated statements of operations
(unaudited)

	Three months ended June 30,		Six months ended June 30,	
	2015	2016	2015	2016
Revenues	$1,288,629	$1,288,629	$3,563,096	$2,577,257
Operating expenses:				
Research and development	9,343,972	19,621,536	17,678,080	37,873,436
General and administrative	6,333,123	10,676,752	10,018,003	19,550,613
Total operating expenses	15,677,095	30,298,288	27,696,083	57,424,049
Loss from operations	(14,388,466)	(29,009,659)	(24,132,987)	(54,846,792)
Interest income	51,624	333,544	62,638	593,966
Net loss	(14,336,842)	(28,676,115)	(24,070,349)	(54,252,826)
Preferred stock dividends	—	—	(634,794)	—
Net loss applicable to common stockholders	$(14,336,842)	$(28,676,115)	$(24,705,143)	$(54,252,826)
Basic and diluted net loss per common share	$(0.60)	$(1.04)	$(1.17)	$(2.00)
Weighted average basic and diluted common shares outstanding	24,080,420	27,456,954	21,031,708	27,132,288
Other comprehensive income (loss):				
Unrealized gain on available-for-sale securities	$—	$70,877	$—	$70,877
Foreign exchange translation adjustment	—	3,253	—	3,253
Total comprehensive income (loss)	$(14,336,842)	$(28,601,985)	$(24,705,143)	$(54,178,696)

See accompanying notes to the unaudited consolidated financial statements.

Spark Therapeutics, Inc.
Consolidated statements of cash flows
(unaudited)

	Six months ended June 30,	
	2015	2016
Cash flows from operating activities:		
Net loss	$(24,070,349)	$(54,252,826)
Adjustments to reconcile net loss to net cash used in operating activities:		
Noncash rent expense	416,052	(361,984)
Depreciation expense	797,177	1,655,788
Stock-based compensation expense	5,458,788	11,513,558
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	(849,073)	(600,446)
Other receivables	(688,669)	15,554,863
Accounts payable and accrued expenses	3,178,565	(1,986,343)
Deferred revenue	(3,563,096)	(2,577,257)
Net cash used in operating activities	(19,320,605)	(31,054,647)
Cash flows from investing activities:		
Purchases of marketable securities	—	(153,954,426)
Payment for acquisition, net of cash acquired	—	(5,911,243)
Purchases of property and equipment	(2,512,357)	(5,652,387)
Net cash used in investing activities	(2,512,357)	(165,518,056)
Cash flows from financing activities:		
Proceeds from exercise of stock options	—	1,044,508
Proceeds from public offerings of common stock, net	170,313,435	127,024,270
Net cash provided by financing activities	170,313,435	128,068,778
Net increase (decrease) in cash and cash equivalents	148,480,473	(68,503,925)
Cash and cash equivalents, beginning of period	74,566,963	293,530,590
Cash and cash equivalents, end of period	$223,047,436	$225,026,665
Supplemental disclosure of cash flow information:		
Deferred financing costs included in other receivables and accounts payable and accrued expenses	$—	$117,317
Property and equipment purchases included in accounts payable and accrued expenses	$247,818	$1,241,453

See accompanying notes to the unaudited consolidated financial statements.

Table of Contents

Spark Therapeutics, Inc.
Notes to consolidated financial statements
(unaudited)

(1) The Company

Spark Therapeutics, Inc. was formed on March 13, 2013 in the state of Delaware as AAVenue Therapeutics, LLC and amended its Certificate of Formation in October 2013 to change its name to Spark Therapeutics LLC. In May 2014, it converted from a limited liability company (LLC) to a C corporation, Spark Therapeutics, Inc. (the Company). The Company is a gene therapy company, seeking to transform the lives of patients suffering from debilitating genetic diseases by developing potentially one-time, life-altering treatments. The Company operates in one segment and has its principal offices in Philadelphia, Pennsylvania.

(a) Follow-on Public Offering

On June 20, 2016, the Company completed a follow-on public offering, having sold 3,025,000 shares of common stock at an offering price of $45.00 per share, for aggregate gross proceeds of $136.1 million. The Company received net proceeds from the public offering of $127.6 million, after deducting underwriting discounts and commissions and other offering expenses.

(2) Development-stage risks

The Company has incurred losses and negative cash flows from operations since inception and had an accumulated deficit of $183.0 million at June 30, 2016. The Company anticipates incurring additional losses until such time, if ever, that it can generate significant sales of its product candidates in development. The Company will need additional financing to fund its operations and to commercially develop its product candidates.

The Company’s future operations are highly dependent on a combination of factors, including: (i) the success of its research and development; (ii) regulatory approval and market acceptance of the Company’s proposed future products; (iii) the timely and successful completion of additional financing; and (iv) the development of competitive therapies by other biotechnology and pharmaceutical companies.

(3) Summary of significant accounting policies

(a) Basis of presentation

The accompanying unaudited interim consolidated financial statements of the Company and its wholly-owned subsidiary have been prepared in accordance with U.S. generally accepted accounting principles (GAAP) for interim financial information. In the opinion of management, the accompanying consolidated financial statements include all normal and recurring adjustments (which consist primarily of accruals, estimates and assumptions that impact the consolidated financial statements) considered necessary to present fairly the Company’s financial position as of June 30, 2016, its results of operations for the three and six months ended June 30, 2015 and 2016 and cash flows for the six months ended June 30, 2015 and 2016. Operating results for the three and six months ended June 30, 2016 are not necessarily indicative of the results that may be expected for the year ending December 31, 2016 or any other period. The interim consolidated financial statements presented herein do not contain the required disclosures under U.S. GAAP for annual consolidated financial statements.

The accompanying unaudited interim consolidated financial statements should be read in conjunction with the annual audited financial statements and related notes as of and for the year ended December 31, 2015 included in the Company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2015.

(b) Use of estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from such estimates.

(c) Fair value of financial instruments

Management believes that the carrying amounts of the Company’s consolidated financial instruments, including cash equivalents, other receivables and accounts payable and accrued expenses, approximate fair value due to the short-term nature of those instruments.

Table of Contents

(d) Property and equipment

Property and equipment consists of computer and laboratory equipment, software, office equipment, furniture and leasehold improvements and is recorded at cost. Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed to operations as incurred. Upon disposal, retirement or sale, the related cost and accumulated depreciation are removed from the accounts and any resulting gain or loss is included in the results of operations. Property and equipment are depreciated on a straight-line basis over their estimated useful lives. The Company uses a life of three years for computer equipment and software, five years for laboratory and office equipment and seven years for furniture. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the asset.

The Company reviews long-lived assets, such as property and equipment, for impairment when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparison of the book values of the assets to estimated undiscounted future cash flows that the assets are expected to generate. If the carrying amount of an asset exceeds its estimated future cash flows, then an impairment charge is recognized for the amount by which the carrying value of the asset exceeds the fair value of the asset.

(e) Research and development

Research and development costs are expensed as incurred. Research and development expenses consist of internal and external expenses. Internal expenses include employee compensation and overhead. External expenses include development, clinical trials, statistical analysis and report writing and regulatory compliance costs incurred with clinical research organizations and other third-party vendors. At the end of the reporting period, the Company compares payments made to third-party service providers to the estimated progress toward completion of the research or development objectives. Such estimates are subject to change as additional information becomes available. Depending on the timing of payments to the service providers and the progress that the Company estimates has been made as a result of the service provided, the Company may record net prepaid or accrued expense relating to these costs. When the Company is reimbursed by a collaboration partner for work performed, the costs incurred are recorded as research and development expenses and the related reimbursement is recorded as a reduction to research and development expenses. Upfront and milestone payments made to third parties who perform research and development services on the Company’s behalf are expensed as services are rendered.

(f) Revenue recognition

The Company has generated revenue solely through license and collaborative agreements. The Company recognizes revenue in accordance with Financial Accounting Standards Board (FASB) Accounting Standards Codification (ASC) Topic 605-25, Revenue Recognition for Arrangements with Multiple Elements, which addresses the determination of whether an arrangement involving multiple deliverables contains more than one unit of accounting. A delivered item within an arrangement is considered a separate unit of accounting only if both of the following criteria are met:

- the delivered item has value to the customer on a stand-alone basis; and
- if the arrangement includes a general right of return relative to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in control of the vendor.

Under FASB ASC Topic 605-25, if both of the criteria above are not met, then separate accounting for the individual deliverables is not appropriate. Revenue recognition for arrangements with multiple deliverables constituting a single unit of accounting is recognized generally over the greater of the term of the arrangement or the expected period of performance, either on a straight-line basis or on a modified proportional performance method.

Milestones related to research and development activities are accounted for in accordance with FASB ASC Topic 605-28, milestone method of revenue recognition. FASB ASC Topic 605-28 allows for the recognition of consideration, which is contingent on the achievement of a substantive milestone in its entirety, in the period the milestone is achieved. A milestone is considered to be substantive if all of the following criteria are met: the milestone is commensurate with either: (1) the performance required to achieve the milestone or (2) the enhancement of the value of the delivered items resulting from the performance required to achieve the milestone; the milestone relates solely to past performance; and the milestone payment is reasonable relative to all of the deliverables and payment

terms within the agreement.

Nonrefundable license fees are recognized as revenue upon delivery provided there are no undelivered elements in the arrangement. For licenses with no stand-alone value, revenues are recognized on a straight-line basis over the related performance period.

Table of Contents

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue on the Company’s consolidated balance sheet. Amounts expected to be recognized as revenue in the next 12 months following the balance sheet date are classified as current liabilities.
To date, the Company has not generated any revenues from the commercial sale of products.

(g) Net loss per common share
Basic and diluted net loss per common share is determined by dividing net loss by the weighted average number of common shares outstanding during the period. For all periods presented unvested restricted shares and common stock options have been excluded from the calculation because their effect would be anti-dilutive. Therefore, the weighted average shares outstanding used to calculate both basic and diluted loss per share are the same.
The following potentially dilutive securities have been excluded from the computations of diluted weighted average shares outstanding as of June 30, 2015 and 2016 as they would be anti-dilutive:

	June 30,	
	2015	2016
Unvested restricted common shares	434,659	326,694
Options issued and outstanding	3,198,697	4,117,256

(h) Deferred rent
Rent expense, including rent holidays and scheduled rent increases, is recorded on a straight-line basis over the term of the lease commencing on the date the Company takes possession of the leased property. Tenant improvement allowances from the lessor are included in the accompanying consolidated balance sheet as deferred rent and are amortized as a reduction of rent expense over the term of the lease from the possession date. Deferred rent as of June 30, 2016 represents the net excess of rent expense over the actual cash paid for rent and the tenant improvement allowances received.

(i) Recent accounting pronouncements

In May 2014, the FASB issued updated guidance regarding the accounting for, and disclosures of, revenue recognition, with an effective date for annual and interim periods beginning after December 15, 2017. The update provides a single comprehensive model for accounting for revenue from contracts with customers. The model requires that revenue recognized reflect the actual consideration to which the entity expects to be entitled in exchange for the goods or services defined in the contract, including in situations with multiple performance obligations. The Company currently is evaluating the effect that this guidance may have on its consolidated financial statements.
In February 2016, the FASB issued ASU 2016-02, “Leases.” ASU 2016-02 requires that lease arrangements longer than 12 months result in an entity recognizing an asset and liability. The updated guidance is effective for interim and annual periods beginning after December 15, 2018, and early adoption is permitted. The Company has not evaluated the impact of the updated guidance on the Company's consolidated financial statements.
In March 2016, the FASB issued ASU 2016-09, "Improvements to Employee Share-Based Payment Accounting". ASU 2016-09 intends to reduce the cost and complexity of accounting for share-based payments. The updated guidance is effective for interim and annual periods beginning after December 15, 2016, and early adoption is permitted. The Company early adopted the guidance as of March 31, 2016 and the impact was immaterial to the Company's consolidated financial statements.

Table of Contents

(4) Marketable securities

The following table summarizes the available-for-sale securities held at June 30, 2016:

Description	Amortized cost	Unrealized gains	Unrealized losses	Fair value
June 30, 2016				
U.S. government agency and corporate securities	$153,954,140	$123,481	$(52,319)	$154,025,302

No available-for-sale securities held as of June 30, 2016 had remaining maturities greater than two years.

(5) Fair value of financial instruments

The Company follows FASB accounting guidance on fair value measurements for financial assets and liabilities measured on a recurring basis. The guidance requires fair value measurements to maximize the use of "observable inputs." The three-level hierarchy of inputs to measure fair value are as follows:

- Level 1: Unadjusted quoted prices in active markets that are accessible at the measurement date for identical, unrestricted assets or liabilities
- Level 2: Significant other observable inputs other than Level 1 prices such as quoted prices in markets that are not active, or inputs that are observable, either directly or indirectly, for substantially the full term of the asset or liability
- Level 3: Prices or valuation techniques that require inputs that are both significant to the fair value measurement and unobservable (i.e., supported by little or no market activity)

The Company has classified assets and liabilities measured at fair value on a recurring basis as follows:

	Fair value measurements at reporting date using		
	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
At December 31, 2015:			
Assets:			
Money market funds (included in cash and cash equivalents)	$293,530,590	—	—
At June 30, 2016:			
Assets:			
Money market funds (included in cash and cash equivalents)	$223,620,269	—	—
Corporate securities (included in cash and cash equivalents)	$1,005,997		
Marketable securities	$154,025,302		

(a) Cash and cash equivalents

The Company considers all highly liquid investments that have maturities of three months or less when acquired to be cash equivalents. Cash equivalents as of June 30, 2016 consisted primarily of money market funds.

(b) Marketable securities

The amortized cost of available-for-sale marketable securities is adjusted for amortization of premiums and accretion of discounts to maturity. At June 30, 2016, the balance in the Company's accumulated other comprehensive income was primarily composed of activity related to the Company's available-for-sale marketable securities. There were no realized gains or losses recognized on the sale or maturity of available-for-sale marketable securities during the three or six months ended June 30, 2016 and, as a result, the Company did not reclassify any amounts out of accumulated other comprehensive income for the same periods.

Table of Contents

(6) Business Acquisition of Genable

On March 7, 2016, the Company acquired Genable Technologies, Ltd. (Genable), an Ireland-based private gene therapy company with which the Company had collaborated since 2014 in the development of Genable's therapeutic program targeting a genetic inherited retinal disease (IRD). With the acquisition, the Company acquired RhoNova™, a potential gene therapy targeting rhodopsin-linked autosomal dominant retinitis pigmentosa (RHO-adRP), an IRD that routinely leads to visual impairment and in the most severe cases to blindness. The consideration paid by the Company to Genable shareholders consisted of $6.1 million in cash and 265,000 shares of the Company's common stock with a fair value of $9.2 million, for total consideration of $15.3 million. In connection with the acquistion, a receivable due from Genable also was settled on the date of acquisition for $0.5 million. The Company incurred acquisition-related costs of approximately $0.3 million, which are included in general and administrative expenses on the consolidated statement of operations for the six months ended June 30, 2016.

The Company has accounted for the acquisition as a business combination under the acquisition method of accounting. The Company has preliminarily allocated the purchase price for the purchase of Genable based upon the estimated fair value of net assets acquired and liabilities assumed at the date of acquisition. The Company expects to finalize the allocation of the purchase price upon receipt of the final valuation for the acquired in-process research and development and goodwill and final resolution of post-closing working capital adjustments. The completion and filing of federal and state tax returns for the purchased entity may result in adjustments to the carrying value of assets and liabilities. Any adjustments to the preliminary fair values will be made as soon as practicable, but not later than one year from the March 7, 2016 acquisition date.

Recognition and measurement of assets acquired and liabilities assumed

The following table summarizes the preliminary fair values of the tangible and intangible assets acquired and liabilities assumed at the acquisition date, net of cash acquired at the acquisition date:

Cash acquired	$196,307
Other current assets	102,506
Acquired in-process research and development	15,490,000
Goodwill	2,096,119
Total assets assumed	17,884,932
Other non-current liabilities	254,753
Deferred tax liability	1,936,250
Total liabilities assumed	2,191,003
Total allocation of purchase price	$15,693,929

Acquired in-process research and development

The Company’s preliminary allocation of purchase price to acquired in-process research and development was $15.5 million. The estimated fair value of the in-process research and development was determined using the “income approach,” which is a valuation technique that provides an estimate of the fair value of an asset based on market participant expectations of the cash flows an asset would generate over its remaining useful life. Some of the more significant assumptions inherent in the development of those asset valuations include the estimated net cash flows for each year for the asset or product (including net revenues, cost of sales, research and development costs, selling and marketing costs and working capital/asset contributory asset charges), the appropriate discount rate to select in order to measure the risk inherent in each future cash flow stream, the assessment of the asset’s life cycle, the potential regulatory and commercial success risks, competitive trends impacting the asset cash flow stream as well as other factors. No assurances can be given that the underlying assumptions used to prepare the discounted cash flow analysis will not change. For these and other reasons, actual results may vary significantly from estimated results.

Table of Contents

(7) Accrued expenses

Accrued expenses consist of the following:

	December 31, 2015	June 30, 2016
Compensation and benefits	$ 4,880,239	$3,472,809
Consulting and professional fees	432,346	1,010,970
Research and development	978,156	1,076,983
Other	238,522	362,042
Total accrued expenses	$ 6,529,263	$5,922,804

(8) Stockholders' equity

The Company's certificate of incorporation and bylaws contain the rights, preferences and privileges of the Company's stockholders and their respective shares. The Company has authorized 150,000,000 shares of common stock and 5,000,000 shares of preferred stock.

(a) Convertible preferred

In 2013 and 2014 the Company issued shares of Series A and Series B convertible preferred stock. Every five shares of Series A Stock and Series B Stock were to automatically convert into one share of common stock at a qualified IPO, as defined, or upon approval by holders of at least 87.5% of the Series B Stock, subject to certain customary antidilution adjustments contained in the Company's certificate of incorporation. The Series A Stock and Series B Stock were entitled to receive cumulative dividends at 8% per annum, which accrued from day to day beginning November 23, 2014 and were payable upon conversion, an event of liquidation or a qualified IPO, in each case, in shares of Series A Stock and Series B Stock, as applicable. As of February 4, 2015, dividends of $1.3 million had accumulated, and in connection with the IPO, were declared and converted along with all outstanding shares of Series A Stock and Series B Stock into an aggregate of 10,200,050 shares of common stock.

(b) Common

In 2013 and 2014, the Company issued restricted stock to various employees, directors and consultants of the Company. The vesting terms of the restricted stock issued varied, but primarily, shares vested 25% on the first anniversary of the vesting commencement date and then quarterly over three years, with accelerated vesting in the event of a change in control, as defined. Any unvested shares are forfeited in the event that the individual ceases to provide services to the Company.

For the six months ended June 30, 2015, the Company recorded compensation expense of $31,616 and $1.4 million in general and administrative expense and research and development expense, respectively, related to the restricted shares. For the six months ended June 30, 2016, the Company recorded compensation expense of $31,538 and $0.7 million in general and administrative expense and research and development expense, respectively, related to the restricted shares.

At June 30, 2016, there was $1.3 million of unrecognized compensation expense related to restricted common shares which is expected to be recognized over a weighted-average period of 1.0 year.

The following table summarizes restricted stock activity:

	Number of shares	Weighted-average grant date fair value
Nonvested shares at December 31, 2015	348,555	$ 4.83
Shares vested	(86,111)	$ 3.90
Nonvested shares at June 30, 2016	262,444	$ 5.14

In February 2015, the Company completed its IPO, having sold 8,050,000 shares of common stock at an IPO price of $23.00 per share, for aggregate gross proceeds of $185.2 million. The Company received net proceeds from the IPO of

$168.9 million,

Table of Contents

after deducting underwriting discounts and commissions and other offering expenses. As part of the IPO, all of the outstanding shares of preferred stock, including shares of preferred stock issued as accrued dividends, were converted into an aggregate of 10,200,050 shares of common stock.

In December 2015, the Company completed a follow-on public offering, having sold 2,266,995 shares of common stock at a public offering price of $47.00 per share, for aggregate gross proceeds of $106.5 million. The Company received net proceeds from the public offering of $99.4 million, after deducting underwriting discounts and commissions and other offering expenses.

In June 2016, the Company completed a follow-on public offering, having sold 3,025,000 shares of common stock at a public offering price of $45.00 per share, for aggregate gross proceeds of $136.1 million. The Company received net proceeds from the public offering of $127.6 million, after deducting underwriting discounts and commissions and other offering expenses.

(9) Stock incentive plans

The Company's 2015 Stock Incentive Plan (the 2015 Plan) provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards to employees, officers, directors, consultants and advisors. In January 2016, the number of shares of common stock authorized for issuance under the 2015 Plan automatically increased, pursuant to the terms of the 2015 Plan, by 1,083,313 shares. As of June 30, 2016, 780,941 shares were available for future grants under the 2015 Plan.

In January 2016, the number of shares of common stock authorized for issuance under the 2015 Employee Stock Purchase Plan (the 2015 ESPP) automatically increased, pursuant to the terms of the 2015 ESPP, by 270,828 shares. The 2015 ESPP will provide participating employees with the opportunity to purchase an aggregate of 490,828 shares of common stock. As of June 30, 2016, no shares were issued under the 2015 ESPP.

The following table summarizes stock option activity:

	Number of options	Weighted-average exercise price
Outstanding at December 31, 2015	3,071,372	$ 22.99
Granted	1,252,850	$ 39.45
Exercised	(187,613)	$ 5.57
Canceled	(19,353)	$ 28.62
Outstanding at June 30, 2016	4,117,256	$ 28.76
Vested at June 30, 2016	973,630	$ 20.35
Vested at June 30, 2016 and expected to vest	4,117,256	$ 28.76

The weighted average remaining contractual term of options outstanding as of June 30, 2016 is 8.7 years. The weighted average remaining contractual term of options vested as of June 30, 2016 is 8.3 years.

During the six months ended June 30, 2015, the Company recorded compensation expense of $1.7 million and $2.1 million in research and development expense and general and administrative expense, respectively, related to stock options.

During the six months ended June 30, 2016, the Company recorded compensation expense of $4.4 million and $5.4 million in research and development expense and general and administrative expense, respectively, related to stock options.

At June 30, 2016, there was $61.1 million of unrecognized compensation expense related to stock options, which is expected to be recognized over a weighted average period of 3.0 years.

The weighted average grant date fair value of the options granted during the six months ended June 30, 2016 was $25.97 per share using the Black-Scholes option-pricing model with the following weighted-average assumptions:

Expected volatility	74.2%

Risk-free interest rate	1.75%
Expected term (in years)	6.08
Expected dividend yield	0.0 %

Table of Contents

The following table summarizes non-vested restricted common stock activity under the 2015 Plan:

	Number of shares	Weighted-average grant date fair value
Nonvested shares at December 31, 2015	25,100	$ 60.03
Shares granted	39,500	$ 43.43
Shares canceled	(350)	$ 60.03
Nonvested shares at June 30, 2016	64,250	$ 49.82

Included in the above table are non-vested restricted stock grants to certain employees and consultants totaling 44,250 shares for which the vesting provisions are based on the achievement of certain Company milestones.

During the six months ended June 30, 2016, the Company recorded compensation expense of $0.5 million and $0.4 million in research and development expense and general and administrative expense, respectively, related to restricted common stock under the 2015 Plan. At June 30, 2016, there was $2.1 million of unrecognized compensation expense related to the restricted common stock.

(10) Related-party transactions

As of December 31, 2015 and June 30, 2016, CHOP was considered a significant equity holder. In October 2013, the Company entered into technology and license agreements with CHOP for certain commercialization licenses to be provided to the Company in order to develop services, methods and marketable products for commercialization. The license agreement requires the Company to reimburse CHOP for the patent costs related to the underlying licensed rights incurred after the effective date. For the three months ended June 30, 2015 and 2016, the Company recorded $0.2 million and $0.2 million, respectively, of general and administrative expense related to the reimbursement of such patent costs in the accompanying consolidated statements of operations. For the six months ended June 30, 2015 and 2016, the Company recorded $0.4 million and $0.5 million, respectively, of general and administrative expense related to the reimbursement of such patent costs in the accompanying consolidated statements of operations.

In 2013, the Company entered into a number of services agreements with CHOP. The Master Research Services Agreement provides for certain research, development, and manufacturing services to be provided to the Company by CHOP. A separate Services Agreement provides for clinical, technical, and administrative services to be provided by CHOP to the Company. For the three months ended June 30, 2015 and 2016, the Company recorded $1.3 million and $1.5 million, respectively, as research and development expense. For the six months ended June 30, 2015 and 2016, the Company recorded $2.2 million and $3.3 million, respectively, as research and development expense.

As of December 31, 2015, $0.2 million and $1.7 million were recorded in accrued expenses and accounts payable, respectively, as amounts due to CHOP. As of June 30, 2016, $0.1 million and $1.2 million were recorded in accrued expenses and accounts payable, respectively, as amounts due to CHOP.

(11) Collaboration and license agreements

In April 2014, the Company began discussions with a biopharmaceutical company concerning a potential manufacturing technology agreement. The Company received a one-time, nonrefundable payment of $1.0 million to engage in due diligence. In March 2015, the Company concluded discussions on a potential arrangement with the biopharmaceutical company and, as a result, the Company recognized the nonrefundable payment of $1.0 million as revenue during the six months ended June 30, 2015.

In December 2014, the Company entered into a global collaboration agreement with Pfizer Inc. (Pfizer), for the development and commercialization of SPK-FIX product candidates for the treatment of hemophilia B. Under the agreement, the Company granted Pfizer an exclusive worldwide license to any Factor IX gene therapy that it develops, manufactures or commercializes prior to December 31, 2024. The Company is primarily responsible for conducting all research and development activities through completion of Phase 1/2 clinical trials of hemophilia B product candidates. Pfizer and the Company will share development costs incurred under an agreed product development plan

for each product candidate with the Company's share of development costs under the agreement limited to $10.6 million. Following the completion of Phase 1/2 clinical trials, Pfizer will be primarily responsible for development, manufacture, regulatory approval and commercialization, including all costs associated therewith. In connection with this agreement, the Company received a $20.0 million upfront payment for the license in December 2014. As there is no stand-alone value for the license, the Company is recognizing revenue through the estimated

Table of Contents

completion date of Phase 1/2 clinical trials. During each of the six month periods ended June 30, 2015 and 2016, the Company recognized $2.6 million of revenue related to the upfront payment. As of June 30, 2016, there is $5.2 million and $6.5 million of current and long term deferred revenue, respectively, related to this payment. During the six month periods ended June 30, 2015 and 2016, the Company recorded $0.8 million and $0.4 million, respectively, as a reduction to research and development expenses for the reimbursement of costs from Pfizer.

The Company is eligible to receive up to an additional $245.0 million in aggregate milestone payments, $125.0 million of which relate to potential development, regulatory and commercial milestones for the first product candidate to achieve each milestone and $120.0 million of which relate to potential regulatory milestones for additional product candidates. In addition, the Company is entitled to receive royalties calculated as a low-teen percentage of net sales of licensed products. The royalties may be subject to certain reductions, including for a specified portion of royalty payments that Pfizer may become required to pay under any third-party license agreements, subject to a minimum royalty. Under the agreement, the Company remains solely responsible for the payment of license payments payable by the Company under specified license agreements.

The agreement will expire on a country-by-country basis upon the latest of: (i) the expiration of the last-to-expire valid claim, as defined in the agreement, in licensed patent rights covering a licensed product; (ii) the expiration of the last-to-expire regulatory exclusivity granted with respect to a licensed product; or (iii) 15 years after the first commercial sale of the last licensed product to be launched, in each case, in the applicable country. Pfizer may terminate the agreement on a licensed product-by-licensed product and country-by-country basis, or in its entirety, for any or no reason subject to notice requirements.

Table of Contents

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

The following discussion and analysis of our financial condition and results of operations should be read together with our 2015 Annual Report on Form 10-K filed with the Securities and Exchange Commission.

Forward-looking statements

This Quarterly Report on Form 10-Q contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Quarterly Report on Form 10-Q, including statements regarding our future results of operations and financial position, business strategy and plans and objectives of management for future operations, are forward-looking statements. The words "may," "will," "should," "expects," "plans," "anticipates," "could," "intends," "target," "projects," "contemplates," "believes," "estimates," "p "potential" or "continue" or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

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

- the timing, scope or likelihood of regulatory filings and approvals, including the timing of our BLA submission for, and final FDA approval of, voretigene neparvovec;
- the timing, progress and results of clinical trials for SPK-CHM, SPK-9001 and our other product candidates, including statements regarding the timing of initiation and completion of clinical trials, dosing of subjects and the period during which the results of the trials will become available;
- our estimates regarding the potential market opportunity for our product candidates;
- the initiation, timing, progress and results of future preclinical studies and clinical trials, and our research and development programs for our other product candidates;
- our ability to achieve milestones and receive payments under our collaborations;
- our plans to develop and commercialize our product candidates;
- our commercialization, medical affairs, marketing and manufacturing capabilities and strategy;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- the scalability and commercial viability of our proprietary manufacturing processes;
- the rate and degree of market acceptance and clinical utility of our product candidates, in particular, and gene therapy in general;
- our competitive position;
- our intellectual property position;
- developments and projections relating to our competitors and our industry;
- our ability to maintain and establish collaborations or obtain additional funding;
- our expectations related to our use of our capital resources;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- the impact of government laws and regulations; and
- our expectations regarding the time during which we will be an Emerging Growth Company under the Jumpstart Our Business Startups Act of 2012, or JOBS Act.

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 Quarterly Report on Form 10-Q, particularly in the "Risk Factors" section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Quarterly Report on Form 10-Q and the documents that we have filed as exhibits to this Quarterly Report on Form 10-Q completely and with the understanding that our actual future results may be materially different from

Table of Contents

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 applicable law.

Overview

We are a leader in the field of gene therapy, seeking to transform the lives of patients suffering from debilitating genetic diseases by developing one-time, life-altering treatments. The goal of gene therapy is to overcome the effects of a malfunctioning, disease-causing gene. Our product candidates have the potential to provide long-lasting effects, dramatically and positively changing the lives of patients with conditions where no, or only palliative, therapies exist. Our initial focus is on treating orphan diseases, and in October 2015 we reported statistically significant results in a pivotal Phase 3 clinical trial of our first product candidate targeting rare genetic blinding conditions, which has received both breakthrough therapy and orphan product designation. Additionally, in May 2016, Pfizer Inc., or Pfizer, and we announced data which show encouraging phase 1/2 initial observations for our hemophilia B candidate.

We also have built a pipeline of product candidates targeting rare blinding conditions, hematologic disorders and neurodegenerative diseases. Our pipeline includes: a product candidate targeting choroideremia currently in a Phase 1/2 clinical trial; product candidates for the treatment of hemophilia including a hemophilia B product candidate currently in a Phase 1/2 clinical trial in collaboration with Pfizer and a preclinical product candidate for hemophilia A to which we retain global commercialization rights; a preclinical product candidate for the treatment of TPP1 deficiency, a form of Batten disease; and other preclinical programs.

Our most advanced product candidate, voretigene neparvovec (formerly referred to as SPK-RPE65), is intended to treat a genetic blinding condition, or inherited retinal disease, or IRD, caused by non sex-linked, or autosomal recessive, mutations in the RPE65 gene. Patients suffering from RPE65-mediated IRD are affected by a range of severe visual impairments, notably night blindness, or nyctolopia, that make independent activities of daily living challenging and ultimately lead to blindness. For example, affected children often depend on visual aids to carry out classroom activities while adults with these diseases may face diminished employment opportunities and may be stripped of some of the rewards of parenting, such as watching a child play his or her favorite sport. We estimate that there are approximately 3,500 individuals with RPE65-mediated IRD in the United States, as well as France, Germany, Italy, Spain and the United Kingdom, which are referred to as the five major European markets. We have received orphan product designation for voretigene neparvovec for the treatment of RPE65-mediated IRD in both the United States and the European Union.

In October 2015, we announced positive top-line results from our pivotal Phase 3 clinical trial of voretigene neparvovec, the first successfully completed randomized controlled Phase 3 trial of a gene therapy for genetic disease in the United States. The trial of 31 subjects met with statistical significance its primary endpoint, the bilateral mobility test change score ($p = .001$), as well as the first two of three secondary endpoints, specifically full-field light sensitivity threshold testing, or FST, ($p < .001$) and the assigned first eye mobility test change score ($p = .001$). Statistical significance was not achieved for the third secondary endpoint, visual acuity ($p = .17$). To date, we have not observed any product candidate-related serious adverse events and no deleterious immune responses in either the Phase 3 trial or in earlier Phase 1 trials. Based on these positive results, we intend to submit a Biologics License Application, or BLA, for voretigene neparvovec with the U.S. Food and Drug Administration, or FDA, as the first step in executing our global regulatory and commercialization strategy. In April 2016, we submitted the non-clinical modules of the BLA to FDA which are the first components of a rolling BLA submission. We currently anticipate that the generation of certain data using validated quality control methods that are part of the chemistry, materials and controls, or CMC, modules of the BLA will occur in early 2017.

The Phase 3 trial demonstrated a statistically significant restoration of vision in subjects that were progressing toward complete blindness. On average, subjects that received voretigene neparvovec demonstrated an improvement of 1.9 light levels one year post-administration. Specifically, nearly two-thirds of the subjects in the intervention group achieved the maximum improvement measurable on the mobility test. Similarly, on average, intervention group subjects achieved a 100-fold improvement in light sensitivity as measured by FST.

In August 2016, we announced positive one-year follow-up data from the Phase 3 trial on the nine control subjects that crossed over after one year and received voretigene neparvovec. Eight of the nine subjects improved as measured by the bilateral mobility test, with all eight responders achieving the maximum improvement measurable. The average

improvement among all nine subjects was 2.1 light levels. As measured by FST, eight of the nine crossover subjects improved, with the average improvement of all nine subjects being nearly 200-fold. There was one serious adverse event in one eye among the nine subjects that was determined to be related to the surgical procedure rather than voretigene neparvovec. This subject exhibited foveal thinning and a reduction in visual acuity after the surgical procedure, which did not return to baseline.

Voretigene neparvovec continues to demonstrate long-lasting effects as measured by both mobility testing and FST. Specifically, a cohort of eight subjects that participated in our second Phase 1 clinical trial, and that would have met the eligibility criteria for the Phase 3 trial, continue to experience durable improvement over three years from time of administration, with observation ongoing. Further, in the continuation of the Phase 3 trial, the original intervention group

Table of Contents

(n = 20) that received voretigene neparvovec demonstrated sustained benefit two years post-treatment as measured by the bilateral mobility test. Average improvement of 1.9 light levels seen at one year was maintained at year two.

We are pursuing other follow-on product candidates targeting other IRDs, including SPK-CHM for the treatment of choroideremia, or CHM. CHM is an IRD linked to the X-chromosome, which manifests in affected males in childhood as night blindness and a reduction of visual field, followed by progressive constriction of visual fields. For CHM patients, it is often in middle age, when people typically are at or near their greatest income-earning potential, that visual impairment begins to limit independent activities of daily living leading to a severe decrease in vision. CHM ultimately results in blindness. We have completed enrollment of subjects in the second cohort of our dose escalating Phase 1/2 trial for SPK-CHM and continue to follow subjects in the trial. To date, SPK-CHM has been well tolerated and we have not observed any product candidate-related serious adverse events in this trial. We have received orphan product designation for SPK-CHM for the treatment of CHM in both the United States and the European Union.

In March 2016, we acquired Genable Technologies Ltd, or Genable, an Ireland-based private gene therapy company with which we had collaborated since 2014 in the development of Genable's therapeutic program targeting a genetic IRD. With the acquisition, we acquired exclusive rights to RhoNova™, a potential targeting rhodopsin-linked autosomal dominant retinitis pigmentosa, or RHO-adRP, an IRD that routinely leads to visual impairment and in the most severe cases to blindness and that we believe affects approximately 12,000 people in the United States and the five major European markets.

In December 2014, we entered into a global collaboration agreement with Pfizer for the development and commercialization of SPK-FIX product candidates for the treatment of hemophilia B. Pfizer and we are developing proprietary, bio-engineered adeno-associated virus, or AAV, vectors utilizing a high-activity FIX transgene and a treatment protocol designed to mitigate immune responses seen in other hemophilia B gene therapy trials, including our own, that have limited the duration of efficacy. Under the terms of the agreement, we received a $20.0 million upfront payment in 2014, earned a $15 million milestone payment in December 2015 and are eligible to receive up to an additional $245.0 million in aggregate milestone payments, as well as royalties calculated as a low-teen percentage of net product sales. Pfizer and we initiated a Phase 1/2 clinical trial of our lead SPK-FIX product candidate, SPK-9001, in 2015. In July 2016, FDA granted breakthrough therapy designation to SPK-9001.

In July 2016, Pfizer and we presented data that demonstrate that the initial-dose cohort of four subjects enrolled in the Phase 1/2 clinical trial of SPK-9001 experienced consistent and sustained factor IX activity levels following a single administration at a dose of 5×10^{11} vg/kg. Across the four subjects, as of July 12, 2016, average steady-state factor IX activity levels were 31.8% ± 6.9%, with a range of range 20% to 44% of normal, determined by averaging levels beginning at eight weeks post-administration through follow-up over 12 to 31 weeks. No sustained elevation in liver enzyme levels above 1.5x the upper limit of normal were seen. To date, SPK-9001 has been well-tolerated and no subjects have needed, or received, immunosuppression. None of the first four subjects, through a combined 76 weeks of observation, has received infusions of factor IX concentrates to prevent bleeding events. Only one precautionary infusion has taken place due to a suspected ankle bleed in one subject two days after administration of vector.

In our SPK-FVIII program for the treatment of hemophilia A, we recently nominated a lead product candidate, SPK-8011, that has demonstrated production of therapeutic levels of Factor VIII in multiple preclinical models at doses that have been safely delivered to humans in hemophilia B studies. We retain global commercialization rights to the SPK-FVIII program.

We are developing a lead neurodegenerative disease product candidate in our SPK-TPP1 program that has demonstrated compelling preclinical proof-of-concept data for the treatment of TPP1 deficiency, a form of Batten disease, a fatal neurological disorder involving mutations of the TPP1 gene, also known as the CLN2 gene, that begins in early childhood. We initiated IND-enabling studies for our lead SPK-TPP1 product candidate in 2015. We have received orphan product designation for SPK-TPP1 for the treatment of of CLN2 disease (neuronal ceroid lipofuscinosis (NCL)) caused by TPP1 deficiency in the United States.

We believe that we have a significant competitive advantage in the field of gene therapy as a result of the collective experience of our scientific and management team and the advanced stage of development of our product candidates. Our scientists and scientific advisors have accumulated over 150 years of collective experience in the field of gene

therapy, contributing key insights and significant developments that have coincided with a resurgence of interest in gene-based medicines. Our proprietary manufacturing processes produce consistent yields of highly pure and stable gene therapies, including both AAV and lentiviral vectors. Our vectors are disarmed viruses that carry genetic material into target cells, where they deliver a functional gene that allows production of a normal protein.

We were formed as AAVenue Therapeutics, LLC, a Delaware limited liability company, on March 13, 2013. On October 14, 2013, we acquired or exclusively in-licensed the commercial and development rights to certain clinical and preclinical programs and intellectual property from CHOP and University of Iowa Research Foundation, or UIRF, and in-licensed additional intellectual property from the University of Pennsylvania, or Penn. On October 15, 2013, we changed our

Table of Contents

name to Spark Therapeutics, LLC. On May 2, 2014, we converted from a Delaware limited liability company into a Delaware corporation, pursuant to which we changed our name to Spark Therapeutics, Inc.

We have never been profitable and have incurred net losses since inception. We have an accumulated deficit of $183.0 million as of June 30, 2016. Substantially all of our net losses resulted from costs incurred in connection with our research and development programs and from general and administrative expenses associated with our operations. For the six months ended June 30, 2015 and 2016, we incurred $17.7 million and $37.9 million of research and development expenses, respectively, and $10.0 million and $19.6 million of general and administrative expenses, respectively.

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, hire additional personnel and initiate commercialization of 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. Even if we are able to generate revenues from the sale of any commercial 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.

Through June 30, 2016, we have received aggregate net proceeds from sales of our equity securities, after deducting underwriting discounts and commissions and other offering expenses payable by us, of $478.3 million. On February 4, 2015, we completed our initial public offering, or IPO, whereby we sold 8,050,000 shares of common stock, inclusive of 1,050,000 shares of common stock sold by us pursuant to the full exercise of an overallotment option granted to the underwriters in connection with the offering, at a price to the public of $23.00 per share. Our shares began trading on the Nasdaq Global Select Market on January 30, 2015. The aggregate net proceeds received by us from the IPO were $168.9 million, net of underwriting discounts and commissions and offering expenses payable by us. Upon the closing of the IPO, all outstanding shares of convertible preferred stock, including accrued dividends, converted into 10,200,500 shares of common stock.

On December 28, 2015, we closed a follow-on offering whereby we sold 2,266,995 shares of common stock at a price to the public of $47.00 per share. The aggregate net proceeds received by us from the follow-on offering were $99.4 million, net of underwriting discounts and commissions and offering expenses payable by us. On June 20, 2016, we closed a follow-on offering whereby we sold 3,025,000 shares of common stock at a price to the public of $45.00 per share. The aggregate net proceeds received by us from the follow-on offering were $127.6 million, net of underwriting discounts and commissions and offering expenses payable by us.

Financial operations overview

Revenue

To date, we have not generated any revenues from product sales. Our revenues have been derived from collaboration agreements.

In April 2014, we entered into discussions with a pharmaceutical company concerning a potential manufacturing technology agreement. We received a one-time, nonrefundable payment of $1.0 million for engaging in due diligence. We concluded discussions on a potential arrangement with the pharmaceutical company in the first quarter of 2015 and, as a result, we recognized the nonrefundable payment of $1.0 million as revenue in the six months ended June 30, 2015.

In December 2014, we entered into a global collaboration agreement with Pfizer for the development and commercialization of product candidates in our SPK-FIX program for the treatment of hemophilia B. Under this collaboration, we maintain responsibility for the clinical development of SPK-FIX product candidates through the completion of Phase 1/2 trials. Thereafter, Pfizer has responsibility for further clinical development, regulatory approvals and commercialization. In connection with entering into this agreement, we received a $20.0 million upfront payment. During each of the six month periods ended June 30, 2015 and 2016, we recognized $2.6 million of revenue and, as of June 30, 2016, there were $5.2 million and $6.5 million of current and long-term deferred revenue, respectively, on our consolidated balance sheet related to this payment.

Our ability to generate product revenue and become profitable depends upon our ability to successfully commercialize products.

Research and development expenses

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

- employee-related expenses, including salaries, benefits, travel and other compensation expenses, including stock-based compensation;

Table of Contents

- expenses incurred under our agreements with contract research organizations, or CROs, and clinical sites that will conduct our preclinical studies and clinical trials and the cost of clinical consultants;
- costs associated with regulatory filings;
- costs of laboratory supplies and the acquiring, developing and manufacturing of preclinical and clinical study materials; and
- costs of facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other operating costs for the portion of our facilities related to research and development.

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

We plan to increase our research and development expenses for the foreseeable future as we continue development of our product candidates. Our current and planned research and development activities include the following:

- completion of non-IND studies required to support the voretigene neparvovec program, including a natural history study;
- expanding our medical affairs group;
- certain pre-launch activities for voretigene neparvovec;
- proposed regulatory submissions for voretigene neparvovec;
- the Phase 1/2 clinical trial for SPK-CHM;
- clinical trials to evaluate the safety and efficacy of SPK-FIX product candidates, initially SPK-9001, that we are developing in collaboration with Pfizer;
- research and development for additional product candidates addressing other IRDs;
- research and development for our preclinical programs for hemophilia A, TPP1 deficiency and other liver and neurodegenerative diseases; and
- continued acquisition and manufacture of clinical trial materials in support of our clinical trials.

The successful development of our product candidates is highly uncertain and subject to numerous risks including, but not limited to:

- the scope, rate of progress and expense of our research and development activities;
- clinical trial results;
- the scope, terms and timing of regulatory approvals;
- the expense of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights;
- the cost, timing and our ability to manufacture sufficient clinical and commercial supplies for any product candidates and products that we may develop; and
- the risks disclosed in the section entitled “Risk Factors” beginning on page 25 of this Quarterly Report on Form 10-Q.

A change in the outcome of any of these variables could mean a significant change in the expenses and timing associated with the development or commercialization of any product candidate.

General and administrative expenses

General and administrative expenses consist primarily of salaries and related costs for personnel, including stock-based compensation and travel expenses, for our employees in executive, operational, finance, legal and human resource functions. Other general and administrative expenses include facility-related costs, professional fees for directors, accounting and legal services, consultants 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 the potential commercialization of our product candidates. We also anticipate continued increased expenses related to costs associated with being a public company, including audit, legal, regulatory and tax-related services associated with maintaining compliance as a public company, director and officer insurance premiums and investor relations costs. Additionally, prior to the potential regulatory approval of our first product candidate, we

Table of Contents

anticipate an increase in payroll and related expenses as a result of our preparation for commercial operations, especially as it relates to sales and marketing.

Results of operations

Comparison of the three months ended June 30, 2015 and 2016

	Three months ended June 30,	
	2015	2016
	(in thousands)	
Revenues	$ 1,289	$ 1,289
Operating expenses:		
Research and development	9,344	19,622
General and administrative	6,333	10,677
Total operating expenses	15,677	30,299
Loss from operations	(14,388)	(29,010)
Interest income	52	334
Net loss	$ (14,336)	$ (28,676)

Revenues

In the three months ended June 30, 2015 and 2016, we recognized $1.3 million and $1.3 million, respectively, of revenue associated with our Pfizer agreement.

Research and development expenses

Our research and development expenses for the three months ended June 30, 2015 were $9.3 million and for the three months ended June 30, 2016 were $19.6 million. The $10.3 million increase was due to a $8.6 million increase in internal research and development expenses, due primarily to significantly increased headcount, and an increase of $1.7 million in external research and development expenses, primarily from an increase of $2.0 million in expenses related to studies for our other product candidates to support our advancing and expanding pipeline, offset by a decrease of $0.3 million associated with our SPK-CHM program.

The following table summarizes our research and development expenses by product candidate or program for the three months ended June 30, 2015 and 2016:

	Three months ended June 30,	
	2015	2016
	(in thousands)	
External research and development expenses:		
Voretigene neparvovec	$ 1,347	$ 1,417
SPK-CHM	513	210
SPK-FIX	478	380
Other product candidates	649	2,638
Total external research and development expenses	2,987	4,645
Total internal research and development expenses	6,357	14,977
Total research and development expenses	$ 9,344	$ 19,622

We do not allocate personnel-related costs, including stock-based compensation, costs associated with broad technology platform improvements or other indirect costs, to specific programs, as they are deployed across multiple projects under development and, as such, are separately classified as internal research and development expenses in the table above.

19

Table of Contents

General and administrative expenses

Our general and administrative expenses for the three months ended June 30, 2015 were $6.3 million and for the three months ended June 30, 2016 were $10.7 million. General and administrative expenses consist primarily of salaries and related costs, including stock-based compensation, legal and patent costs and other professional fees. The $4.4 million increase was primarily due to an increase of $3.2 million in salaries and related costs, including stock-based compensation, due to increased headcount and an increase of $1.2 million in legal and patent expenses, professional fees and other operating costs.

Comparison of the six months ended June 30, 2015 and 2016

	Six months ended June 30,	
	2015	2016
	(in thousands)	
Revenues	$ 3,563	$ 2,577
Operating expenses:		
Research and development	17,678	37,873
General and administrative	10,018	19,551
Total operating expenses	27,696	57,424
Loss from operations	(24,133)	(54,847)
Interest income	63	594
Net loss	$ (24,070)	$ (54,253)

Revenues

In the six months ended June 30, 2015, we recognized $2.6 million of revenue associated with our Pfizer agreement and $1.0 million associated with a non-refundable payment from a biopharmaceutical company received in 2014 for a potential manufacturing technology agreement that did not occur. Discussions on the potential agreement concluded in March 2015.

In the six months ended June 30, 2016, we recognized $2.6 million of revenue associated with our Pfizer agreement.

Research and development expenses

Our research and development expenses for the six months ended June 30, 2015 were $17.7 million and for the six months ended June 30, 2016 were $37.9 million. The $20.2 million increase was due to a $15.4 million increase in internal research and development expenses, due primarily to significantly increased headcount, and an increase of $4.8 million in external research and development expenses, primarily from an increase of $1.8 million in expenses related to studies to support, and certain pre-launch activities for, voretigene neparvovec and $3.9 million related to other product candidates to support our advancing and expanding pipeline, offset by a decrease of $0.6 million associated with our SPK-FIX program and $0.3 million associated with our SPK-CHM program.

Table of Contents

The following table summarizes our research and development expenses by product candidate or program for the six months ended June 30, 2015 and 2016:

	Six months ended June 30,	
	2015	2016
	(in thousands)	
External research and development expenses:		
Voretigene neparvovec	$ 2,325	$ 4,083
SPK-CHM	962	640
SPK-FIX	1,182	603
Other product candidates	1,094	5,018
Total external research and development expenses	5,563	10,344
Total internal research and development expenses	12,115	27,529
Total research and development expenses	$ 17,678	$ 37,873

We do not allocate personnel-related costs, including stock-based compensation, costs associated with broad technology platform improvements or other indirect costs, to specific programs, as they are deployed across multiple projects under development and, as such, are separately classified as internal research and development expenses in the table above.

General and administrative expenses

Our general and administrative expenses for the six months ended June 30, 2015 were $10.0 million and for the six months ended June 30, 2016 were $19.6 million. General and administrative expenses consist primarily of salaries and related costs, including stock-based compensation, legal and patent costs and other professional fees. The $9.6 million increase primarily was due to an increase of $6.2 million in salaries and related costs, including stock-based compensation, due to increased headcount and an increase of $3.4 million in legal and patent expenses, professional fees and other operating costs.

Liquidity and capital resources

The following table sets forth the primary sources and uses of cash and cash equivalents for each period set forth below:

	Six months ended June 30,	
	2015	2016
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$ (19,321)	$ (31,055)
Investing activities	(2,512)	(165,518)
Financing activities	170,313	128,069
Net increase (decrease) in cash and cash equivalents	$ 148,480	$ (68,504)

Net cash used in operating activities

The net cash used in operating activities was $19.3 million for the six months ended June 30, 2015, and consisted of a net loss of $24.1 million adjusted for non-cash items, including depreciation expense of $0.8 million, stock-based compensation expense of $5.5 million, non-cash rent expense of $0.4 million and a net increase in operating assets and liabilities of $1.9 million. The significant items in the change in operating assets and liabilities include a decrease in deferred revenue of $3.6 million, of which $2.6 million is related to our Pfizer agreement and $1.0 million is related to the non-refundable payment received for engaging in due diligence with a potential manufacturing technology partner, and an increase of $3.2 million in accounts payable and accrued expenses and an increase of $1.5 million in prepaid expenses and other assets.

The net cash used in operating activities was $31.1 million for the six months ended June 30, 2016, and consisted of a net loss of $54.3 million adjusted for non-cash items, including depreciation expense of $1.7 million, stock-based

compensation expense of $11.5 million, non-cash rent expense of $0.4 million and a net decrease in operating assets and liabilities of $10.4 million. The significant items in the change in operating assets and liabilities include a decrease in other receivable of $15.5

Table of Contents

million, of which $15.0 million is related to payment due from Pfizer and an increase of $0.6 million in prepaid expenses and other assets, offset by a decrease in accounts payable and accrued expenses of $2.0 million and deferred revenue of $2.6 million.

Net cash used in investing activities

Net cash used in investing activities for the six months ended June 30, 2015 was $2.5 million, consisting of costs related to the purchase of property and equipment.

Net cash used in investing activities for the six months ended June 30, 2016 was $165.5 million, consisting of purchases of marketable securities of $154.0 million, costs related to the purchase of property and equipment of $5.6 million and $5.9 million of cash consideration for the acquisition of Genable, net of cash acquired.

Net cash provided by financing activities

Net cash provided by financing activities for the six months ended June 30, 2015 was $170.3 million, which represents the proceeds from the issuance of common stock in our IPO, net of expenses.

Net cash provided by financing activities for the six months ended June 30, 2016 was $128.1 million, which consisted of $127.7 million of net proceeds from our follow-on public offering in June 2016 and $1.1 million from the exercise of stock options during the first half of 2016, offset by expenses of $0.7 million paid in the first quarter of 2016 related to our follow-on offering in December 2015.

Funding requirements

We expect our expenses to increase compared to prior periods in connection with our ongoing activities, particularly as we continue research and development, continue and initiate clinical trials and seek regulatory approvals for our product candidates. In anticipation of regulatory approval for any of our product candidates, we expect to incur significant pre-launch expenses.

The expected use of our cash, cash equivalents and marketable securities of $379.1 million as of June 30, 2016 represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development programs, the status of, and results from, clinical trials, the potential need to conduct additional clinical trials to obtain approval of our product candidates for all intended indications, as well as any technology acquisitions or additional collaborations into which we may enter with third parties for our product candidates and any unforeseen cash needs. As a result, our management retains broad discretion over the allocation of our existing cash and cash equivalents and the net proceeds from this offering. Based on our planned use of our cash, cash equivalents and marketable securities, we estimate that such funds will be sufficient to enable us to complete the submission of a BLA and prepare for commercialization of voretigene neparvovec, complete our Phase 1/2 trial for SPK-CHM, complete our Phase 1/2 trial of SPK-9001 in collaboration with Pfizer, continue ongoing development of our SPK-FVIII program for the treatment of hemophilia A, advance certain of our other pipeline product candidates and fund our operating expenses and capital expenditure requirements into 2019. The foregoing estimate does not contemplate the receipt of any milestone payments under our collaboration with Pfizer. Moreover, we have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect.

Off-balance sheet arrangements

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

Contractual obligations

There were no material changes to our contractual obligations and commitments described under Management’s Discussion and Analysis of Financial Condition and Results of Operations in the Annual Report on Form 10-K for the year ended December 31, 2015.

22

Table of Contents

Critical accounting policies and significant judgments and estimates

Management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reporting amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued expenses and stock-based compensation. We base our estimates on historical experience, known trends and events and various other factors that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Except as noted below, there have been no material changes to our critical accounting policies from those described in "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in our Annual Report on Form 10-K, which was filed with the Securities and Exchange Commission on March 14, 2016.

Impairment of Goodwill and Indefinite-lived Intangible Assets

As a result of the Genable acquisition, we are required to review, on an annual basis, the carrying value of goodwill and indefinite-lived intangible assets, to determine whether impairment may exist. For goodwill, the two-step goodwill impairment test consists of the following steps. The first step compares a reporting unit's fair value to its carrying amount to identify potential goodwill impairment. If the carrying amount of a reporting unit exceeds the reporting unit's fair value, the second step of the impairment test must be completed to measure the amount of the reporting unit's goodwill impairment loss, if any. Step two requires an assignment of the reporting unit's fair value to the reporting unit's assets and liabilities to determine the implied fair value of the reporting unit's goodwill. The implied fair value of the reporting unit's goodwill is then compared with the carrying amount of the reporting unit's goodwill to determine the goodwill impairment loss to be recognized, if any. The impairment test for indefinite-lived intangible assets is a one-step test, which compares the fair value of the intangible asset to its carrying value. If the carrying value exceeds its fair value, an impairment loss is recognized in an amount equal to the excess. Based on accounting standards, it is required that these assets be assessed at least annually for impairment unless a triggering event occurs between annual assessments which would then require an assessment in the period in which a triggering event occurred.

Item 3. Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risk related to changes in interest rates. As of June 30, 2016, we had cash, cash equivalents and marketable securities of $379.1 million, primarily invested in U.S. government agency and corporate securities, cash and money market accounts. We have policies requiring us to invest in the securities of high-quality issuers, limit our exposure to any individual issuer and ensure adequate liquidity. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Our marketable securities are subject to interest rate risk and will fall in value if market interest rates increase. If market interest rates were to increase immediately and uniformly by 100 basis points from levels at June 30, 2016, the net fair value of our marketable securities would have resulted in a hypothetical decline of approximately $0.6 million.

Item 4. Controls and Procedures

Evaluation of disclosure controls and procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of June 30, 2016. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission's rules and forms. Disclosure controls and

procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that

Table of Contents

any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of June 30, 2016, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in internal control over financial reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the quarter ended June 30, 2016 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Table of Contents

PART II. OTHER INFORMATION

Item 1. Legal Proceedings
We currently are not subject to any material legal proceedings.

Item 1A. Risk Factors
The following risk factors and other information included in this Quarterly Report on Form 10-Q should be carefully considered. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 13 of this Quarterly Report on Form 10-Q for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks related to our financial position
We have incurred net losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.
Since inception, we have incurred net losses. Our net losses were $24.7 million and $54.2 million for the six months ended June 30, 2015 and 2016, respectively. As of June 30, 2016, we had an accumulated deficit of $183.0 million. We have financed our operations primarily through private placements of our preferred stock, our IPO, which closed on February 4, 2015, and two follow-on offerings, which closed on December 21, 2015 and June 20, 2016. We received net proceeds from the IPO and follow-on offerings of $395.9 million, after deducting underwriting discounts and commissions and other offering expenses payable by us. We have devoted substantially all of our efforts to research and development, including clinical and preclinical development of our product candidates, as well as to building out our team. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if, and as, we:
- prepare our BLA and marketing authorization application, or MAA, for voretigene neparvovec and seek marketing approvals for any of our other product candidates that successfully complete clinical trials;
- continue our clinical development of our product candidates, including our Phase 1/2 clinical trials for SPK-CHM and SPK-9001;
- continue IND-enabling studies and commence Phase 1/2 clinical trials for our SPK-FVIII and SPK-TPP1 programs;
- initiate additional preclinical studies and clinical triails for our other product candidates;
- seek to identify additional product candidates;
- validate a commercial-scale current good manufacturing practices, or cGMP, manufacturing facility;
- build out additional laboratory and cGMP manufacturing capacity;
- further develop our gene therapy platform;
- expand our medical affairs efforts;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio; and
- acquire or in-license other product candidates and technologies.

To become and remain profitable, we must develop and eventually commercialize product candidates with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products for which we may obtain marketing approval and satisfying any post-marketing requirements. We may never succeed in any or all of these activities and, even if we do, we may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital,

maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company also could cause our stockholders to lose all or part of their investment.

We have never generated revenue from product sales and may never be profitable.

Our ability to generate revenue from product sales and achieve profitability depends on our ability, alone or with collaborative 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 the next several years, if ever. Our ability to generate future revenues from product sales depends heavily on our, or our collaborators', success in:

- completing research and preclinical and clinical development of our product candidates and identifying new gene therapy product candidates;
- seeking and obtaining regulatory and marketing approvals for product candidates for which we complete clinical trials;
- launching and commercializing product candidates for which we obtain regulatory and marketing approval by establishing a sales force, marketing and distribution infrastructure or, alternatively, collaborating with a commercialization partner;
- qualifying for adequate coverage and reimbursement by government and third-party payors for our product candidates;
- maintaining and enhancing a sustainable, scalable, reproducible and transferable manufacturing process for our vectors and product candidates;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and the market demand for our product candidates, if approved;
- obtaining market acceptance of our product candidates as a viable treatment option;
- addressing any competing technological and market developments;
- implementing additional internal systems and infrastructure, as needed;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter and performing our obligations in such collaborations;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- avoiding and defending against third-party interference or infringement claims; and
- attracting, hiring and retaining qualified personnel.

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 FDA, European Medicines Agency, or EMA, or other regulatory authorities to perform clinical 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 limited operating history may make it difficult for stockholders to evaluate the success of our business to date and to assess our future viability.

We were founded in March 2013. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring our technology, identifying potential product candidates and undertaking preclinical studies and clinical trials of our most advanced product candidates and establishing collaborations. We have not yet demonstrated the ability to obtain marketing approvals, manufacture a commercial-scale product or conduct sales and marketing activities necessary for successful commercialization. Consequently, any predictions stockholders make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition from a company with a research focus to a company that is also capable of supporting commercial activities. We may not be successful in such a transition.

25

Table of Contents

We may need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate certain of our product development efforts or other operations.

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate further clinical trials of and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant expenses related to product sales, medical affairs, marketing, manufacturing and distribution. Furthermore, we expect to continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate certain of our research and development programs.

Our operations have consumed significant amounts of cash since inception. As of June 30, 2016, our cash and cash equivalents and marketable securities were $379.1 million. Our research and development expenses increased from $17.7 million for the six months ended June 30, 2015 to $37.9 million for the six months ended June 30, 2016. We estimate that our cash and cash equivalents and marketable securities as of June 30, 2016 will enable us to fund our operating expenses and capital expenditure requirements into 2019.

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

- the costs of preparing and filing a BLA with FDA and an MAA with EMA for voretigene neparvovec;
- the cost and our ability to establish commercial infrastructure and manufacturing capabilities required to support the launch of voretigene neparvovec;
- whether additional clinical testing is required to secure regulatory approvals for all intended or desired indications of voretigene neparvovec;
- the scope, progress, results and costs of drug discovery, recruitment, laboratory testing, preclinical development and clinical trials for our other product candidates;
- the costs associated with the build out of additional laboratory and cGMP manufacturing capacity;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- revenue, if any, received from commercial sale of our products, including amounts reimbursed by government and third party payors should any of our product candidates receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our current collaboration agreements remaining in effect and our achievement of milestones under those agreements;
- our ability to establish and maintain additional collaborations on favorable terms, if at all; and
- the extent to which we acquire or in-license other product candidates and technologies.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our product revenues, if any, and any commercial milestones or royalty payments under our collaboration agreements, will be derived from or based on sales of products that may not be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. To the extent that additional capital is raised through the sale of equity or equity-linked securities, the issuance of those securities could result in substantial dilution for our current stockholders and the terms may include liquidation or other preferences that adversely affect the rights of our current stockholders. Furthermore, the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our common stock to decline and existing stockholders may not agree with our financing plans or the terms of such financings. Adequate additional financing may not be available to us on acceptable terms, or at all.

26

Table of Contents

Risks related to the development of our product candidates

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

We have concentrated our research and development efforts on our gene therapy platform, and our future success depends on our successful development of viable gene therapy product candidates. There can be no assurance that we will not experience problems or delays in developing new product candidates and that such problems or delays will not cause unanticipated costs, or that any such development problems can be solved. Although we intend to leverage our experience with voretigene neparvovec, we may be unable to reduce development timelines and costs for our other IRD gene therapy development programs. We also may experience unanticipated problems or delays in expanding our manufacturing capacity, which may prevent us from completing our clinical trials, meeting the obligations of our collaborations or commercializing our products on a timely or profitable basis, if at all. For example, we, a collaborator or another group may uncover a previously unknown risk associated with AAV, and this may prolong the period of observation required for obtaining regulatory approval or may necessitate additional clinical testing.

In addition, the clinical trial requirements of FDA, EMA and other regulatory authorities 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 more extensively studied product candidates. Only one gene therapy product for a genetic disease, uniQure N.V.’s Glybera, has received marketing authorization from the European Commission. It is 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 the European Union or how long it will take to commercialize our product candidates. Approvals by the European Commission may not be indicative of what FDA may require for approval.

Regulatory requirements governing gene and cell therapy products have changed frequently and may continue to change in the future. FDA has established the Office of Cellular, Tissue and Gene Therapies within the Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER in its review. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from U.S. National Institutes of Health, or NIH, also potentially are subject to review by the NIH office of Biotechnology Activities' Recombinant DNA Advisory Committee, or RAC; however, NIH recently announced that the RAC will soon only publicly review clinical trials if the trials cannot be evaluated by standard oversight bodies and pose unusual risks. Although FDA decides whether individual gene therapy protocols may proceed, the RAC public review process, if undertaken, can delay the initiation of a clinical trial, even if FDA has reviewed the trial design and details and approved its initiation. Conversely, FDA can put an Investigational New Drug exemption, or IND, on a clinical hold even if the RAC has provided a favorable review or an exemption from in-depth, public review. If we were to engage an NIH-funded institution, such as CHOP, to conduct a clinical trial, that institution’s institutional biosafety committee as well as its institutional review board, or IRB, would need 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 FDA or other oversight bodies to change the requirements for approval of any of our product candidates. Similarly, EMA may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal products and require that we comply with these new guidelines.

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 certain of our product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. 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, and our business, financial condition, results of operations and prospects would be materially and adversely affected.

The results from our pivotal Phase 3 clinical trial for voretigene neparvovec may not support as broad a marketing approval as we seek, and FDA and EMA may require us to conduct additional clinical trials or evaluate subjects for an additional follow-up period.

While we believe voretigene neparvovec should be applicable for the treatment of patients with any IRD mediated by RPE65 mutations, the results from our pivotal Phase 3 clinical trial for voretigene neparvovec, which included only subjects diagnosed with LCA due to RPE65 mutations, may not support as broad a marketing approval as we seek. Even if we obtain

Table of Contents

regulatory approval for voretigene neparvovec, we might obtain marketing approval only to treat patients diagnosed with LCA due to RPE65 mutations, based on the inclusion criteria of the Phase 3 trial and the absence of data for patients diagnosed with RPE65-mediated IRDs other than LCA. If voretigene neparvovec is not approved for RPE65-mediated IRDs other than LCA, we may be required by FDA and EMA to conduct additional clinical trials to support approval of voretigene neparvovec for patients with patients diagnosed with RP due to RPE65 mutations or other RPE65-mediated IRDs. This could result in our experiencing substantial delays in obtaining, or never obtaining, marketing approval for voretigene neparvovec to treat patients diagnosed with RP due to RPE65 mutations or other RPE65-mediated IRDs. The inability to market voretigene neparvovec to treat patients with these other clinical classifications would have a material adverse effect on our projected revenues from voretigene neparvovec and our business, financial condition, results of operations and prospects.

Because we are developing product candidates for the treatment of diseases in which there is little clinical experience and, in some cases, using new endpoints or methodologies, there is increased risk that FDA or other regulatory authorities may not consider the endpoints of our clinical trials, including our Phase 3 clinical trial for voretigene neparvovec, to provide clinically meaningful results.

There are no pharmacologic therapies approved to treat IRDs caused by autosomal recessive mutations to the RPE65 gene or mutations to the CHM gene. In addition, there has been limited clinical trial experience for the development of pharmaceuticals to treat IRDs. Certain aspects of IRDs render efficacy endpoints historically used for vision clinical trials less applicable as clinical endpoints. As a result, the design and conduct of clinical trials for these disorders is subject to increased risk.

FDA described, in general terms, the criteria by which it will judge the validity of the primary efficacy endpoint we chose for our pivotal Phase 3 clinical trial of voretigene neparvovec. FDA has communicated that guidance through comments on our request for a Special Protocol Assessment, or SPA, which was submitted in 2009, and during subsequent regulatory meetings. FDA stated that the primary endpoint should be clinically meaningful, reflecting a tangible benefit to patients. Further, FDA stated that, preferably, the benefit would improve quality of life, a standard that can be difficult to validate. We voluntarily withdrew our SPA submission at FDA's request to allow FDA more time for a comprehensive assessment of the Phase 3 trial design. A subsequent Advisory Committee in June 2011 addressed a number of these elements. EMA's only comment on the validity of the primary endpoint for our pivotal Phase 3 clinical trial was to use only the binocular testing condition. There can be no assurances that FDA or EMA will not have additional questions or comments with respect to our data analyses or any of the endpoints of our Phase 3 trial or that we will adequately address any questions or comments that they may have.

We developed a mobility test of functional vision that measures subjects' ability to navigate a specially designed course at incrementally reduced lighting conditions. The subjects follow black arrows on white tiles on the floor around the course, while avoiding common obstacles such as waste baskets. This mobility test is designed to measure improvements in peripheral vision and improvements in night blindness. These are two predominant visual deficits in patients with RPE65-mediated IRDs. The mobility test for our pivotal Phase 3 clinical trial of voretigene neparvovec used seven decreasing increments of light designed to correspond to light conditions encountered during daily activities and in common environments, such as the interior of a shopping mall, the inside of a stairwell and an outdoor parking lot at night. We defined our primary efficacy endpoint as the ability to navigate the course accurately within a given timeframe, at one or more lighting levels lower than the level at which a subject previously had been able to complete the course.

At an FDA advisory committee meeting on gene therapy products for the treatment of retinal disorders convened by CBER in June 2011, we presented a summary of our clinical data to date, as well as our then-proposed Phase 3 trial design. In May 2012, reviewers from FDA, CBER and several ophthalmologists from FDA provided feedback on our proposed mobility test stating that improvement in the ability to navigate at a lower lighting condition may represent an improvement in visual function. FDA requested that we justify a change score on the endpoint that would reliably confer clinical benefit and power our trial accordingly. In the protocol for the Phase 3 trial submitted to FDA, we described in detail our primary endpoint based on a change score of positive one or more light levels. FDA allowed our clinical trial to proceed using that endpoint, even though FDA has authority to place a clinical trial on hold if the protocol for an investigation is "clearly deficient" in design to meet its stated objectives. Through continuing dialogue

pursuant to the breakthrough therapy designation of voretigene neparvovec, we modified the designation of pupillary light reflex to be an exploratory endpoint and the analysis of the mobility test change score for an assigned first eye became a secondary endpoint, resulting in three secondary endpoints: full-field light sensitivity threshold testing, the assigned first eye mobility test change score and visual acuity.

Even though we achieved statistical significance in the pre-specified primary mobility test endpoint and the first two secondary efficacy endpoints, FDA has discretion to reserve judgment on whether the endpoints and the change scores seen in our trial sufficiently demonstrate clinical meaningfulness, including the weight FDA places on the secondary endpoint visual acuity, which was not met to a degree of statistical significance, until FDA reviews our BLA. FDA also weighs the benefits of a product against its risks and FDA may view the efficacy results in the context of safety as not being supportive of regulatory

Table of Contents

approval. Other regulatory authorities in the European Union and other countries may make similar comments with respect to these endpoints.

Additionally, for the Phase 3 trial, we enrolled subjects as young as four years of age (compared to subjects as young as eight years of age in our earlier Phase 1 trials). Even though both arms of the Phase 3 trial were balanced as to age, there is a risk that regulators may question whether subjects at this age could demonstrate improvement in the mobility test as a result of their cognitive development, and not due to voretigene neparvovec. The mobility test is not designed to detect the extent to which improvement is a result of cognitive development versus the impact of voretigene neparvovec, therefore, potentially calling into question efficacy results for younger-age subjects. Further, while certain of our secondary endpoints, such as measuring visual acuity, traditionally have been used in clinical settings, due to the unique deficits faced by subjects with IRDs, these traditional tests may not adequately assess patients' ability to independently carry out activities of daily living. As a result of any of the above, FDA may decide that our results are not clinically meaningful which could delay or prevent approval of voretigene neparvovec, and could result in FDA or other regulatory authorities requiring us to conduct additional clinical trials.

In addition, the treatment of certain IRDs, such as CHM, may require assessment of clinical endpoints that reflect a stabilization, as opposed to an improvement, of functional vision. Assessing these endpoints may require longer periods of observation and may delay the completion of any trials we may undertake.

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

Results from preclinical studies or previous clinical trials are not necessarily predictive of future clinical trial results, and interim results of a clinical trial are not necessarily indicative of final results. Our product candidates may fail to show the desired safety and efficacy in clinical development despite demonstrating positive results in preclinical studies or having successfully advanced through initial clinical trials. For example, after multiple successful preclinical studies using gene therapy to treat hemophilia B, several hemophilia B product candidates, including product candidates we previously evaluated, have produced sub-optimal durability in Phase 1 trials.

We have limited safety and no clinical efficacy data for the use of SPK-CHM in humans. We have limited safety and clinical efficacy data for the use of SPK-9001 in humans. In addition, we have no clinical data demonstrating either the safety or efficacy of our current SPK-FVIII or SPK-TPP1 product candidates in humans. There can be no assurance that the success we achieved in the preclinical studies for any of our product candidates ultimately will result in success in our planned clinical trials. In addition, there can be no assurance that we will be able to achieve the same or similar success in our preclinical studies and clinical trials of our other product candidates.

There is a high failure rate for drugs and biologic products proceeding through clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and 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. Any such delays could materially and adversely affect our business, financial condition, results of operations and prospects.

We may find it difficult to enroll patients in our clinical trials, which could delay or prevent us from proceeding with 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 our ability to recruit patients to participate as well as completion of required follow-up periods. For example, hemophilia trials often take longer to enroll than trials for other indications due to the availability of existing treatments. We have experienced slow enrollment in some of our prior hemophilia trials, and we may experience similar delays in any of our current or future clinical trials. In addition, the small number of patients with Batten disease and efforts by competitors to conduct clinical trials for their product candidates in the same indication may hamper our ability to enroll a sufficient number of patients in any future clinical trials of SPK-TPP1. If patients are unwilling to participate in our gene therapy studies because of negative publicity from adverse events related to the biotechnology or gene therapy fields, competitive clinical trials for similar patient populations, clinical trials in products employing our vectors or our platform or for other reasons, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of our product candidates may be delayed.

These delays could result in increased costs, delays in advancing our product candidates, delays in testing the effectiveness of our product candidates or termination of the clinical trials altogether.

Table of Contents

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics, to complete our clinical trials in a timely manner. Patient enrollment and trial completion is affected by factors including:

- size of the patient population and process for identifying subjects;
- design of the trial protocol;
- eligibility and exclusion criteria;
- perceived risks and benefits of the product candidate under study;
- perceived risks and benefits of gene therapy-based approaches to treatment of diseases;
- availability of competing therapies and clinical trials;
- severity of the disease under investigation;
- availability of genetic testing for potential patients;
- proximity and availability of clinical trial sites for prospective subjects;
- ability to obtain and maintain subject consent;
- risk that enrolled subjects will drop out before completion of the trial;
- patient referral practices of physicians; and
- ability to monitor subjects adequately during and after treatment.

Our current product candidates are being developed to treat rare conditions. We plan to seek initial marketing approvals in the United States and the European Union. 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 FDA or EMA or other 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 CROs and physicians;
- different standards for the conduct of clinical trials;
- absence in some countries of established groups with sufficient regulatory expertise for review of gene therapy protocols;
- 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 treatment.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business, financial condition, results of operations and prospects.

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 the product candidates. 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 reaching a consensus with regulatory authorities on trial design;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites;
- delays in opening clinical trial sites or obtaining required Institutional Review Board, or IRB, or independent Ethics Committee approval at each clinical trial site;
- delays in recruiting suitable subjects to participate in our clinical trials;
- imposition of a clinical hold by regulatory authorities as a result of a serious adverse event or after an inspection of our clinical trial operations or trial sites;

Table of Contents

- failure by us, any CROs we engage or any other third parties to adhere to clinical trial requirements;
- failure to perform in accordance with FDA good clinical practices, or GCP, or applicable regulatory guidelines in the European Union and other countries;
- delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical sites, including delays by third parties with whom we have contracted to perform certain of those functions;
- delays in having subjects complete participation in a trial or return for post-treatment follow-up;
- clinical trial sites or subjects dropping out of a trial;
- selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;
- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- occurrence of serious adverse events in trials of the same class of agents conducted by other sponsors; or
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

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 make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays also could 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, financial condition, results of operations and prospects.

Additionally, if the results of our clinical trials are inconclusive or if there are safety concerns or serious 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 in 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, or suspend, 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.

Our product candidates and the process for administering our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial potential or result in significant negative consequences following any potential marketing approval.

There have been several significant adverse side effects in gene therapy treatments in the past, including reported cases of leukemia and death seen in other trials using other vectors. While new recombinant vectors have been developed to reduce these side effects, gene therapy is still a relatively new approach to disease treatment and additional adverse side effects could develop. There also is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biologic activity of the genetic material or other components of products used to carry the genetic material.

Possible adverse side effects that could occur with treatment with gene therapy products include an immunologic reaction early after administration which, while not necessarily adverse to the patient’s health, could substantially limit the effectiveness of the treatment. In previous clinical trials involving AAV vectors for gene therapy, some subjects experienced the development of a T-cell response, whereby after the vector is within the target cell, the cellular immune response system triggers the removal of transduced cells by activated T-cells. If our vectors demonstrate a similar effect we may decide or be required to halt or delay further clinical development of our product candidates.

Table of Contents

In addition to any potential side effects caused by the product candidate, the administration process or related procedures also can cause adverse side effects. If any such adverse events occur, our clinical trials could be suspended or terminated. For example, FDA placed our second open-label Phase 1 clinical trial, which we refer to as our 102 trial, on a clinical hold temporarily when we voluntarily halted enrollment and reported a serious adverse event arising from a steroid injection given following administration of voretigene neparvovec to manage post-operative inflammation related to the standard vitrectomy procedure subjects undergo prior to administration of voretigene neparvovec. We subsequently adjusted the protocol regarding the use of local steroids and FDA released the clinical hold, allowing the trial to proceed.

If in the future we are unable to demonstrate that such adverse events were caused by the administration process or related procedures, FDA, the European Commission, EMA or other regulatory authorities could order us to cease further development of, or deny approval of, our product candidates for any or all targeted indications. Even if we are able to demonstrate that all future serious adverse events are not product-related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, 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 may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to develop other product candidates, and may harm our business, financial condition and prospects significantly.

Additionally, if any of our product candidates receives marketing approval, 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 the product 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, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product candidate;
- regulatory authorities may require additional warnings on the label;
- 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 additional orphan drug designations or orphan drug exclusivity for any product. If our competitors are able to obtain orphan drug exclusivity for products that constitute the same drug and treat the same indications as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as having a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the European Union, EMA’s Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than 5 in 10,000 persons in the European Union. Additionally, orphan designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biologic product.

Voretigene neparvovec has been granted orphan drug designation by FDA and the European Commission for the treatment of both LCA and RP due to RPE65 mutations. SPK-CHM has been granted orphan drug designation by FDA and the European Commission for the treatment of choroideremia. SPK-TPP1 has been granted orphan product

designation by FDA for the treatment of of CLN2 disease (neuronal ceroid lipofuscinosis (NCL)) caused by TPP1 deficiency.

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

Table of Contents

granted orphan product designation by the European Commission and FDA for its product candidate for the treatment of choroideremia that is in a Phase 1/2 clinical trial.

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

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

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

Breakthrough therapy designation by FDA may not lead to a faster development, regulatory review or approval process, and it does not increase the likelihood that any of our product candidates will receive marketing approval in the United States.

We have received breakthrough therapy designation for voretigene neparvovec for nyctalopia in patients with LCA due to RPE65 mutations, as confirmed by genetic testing. We have received breakthrough therapy designation for SPK-9001 for the treatment of hemophilia B. We may, in the future, apply for breakthrough therapy designation for other product candidates in the United States. A breakthrough therapy product candidate is defined as a product candidate that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that such product candidate may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. FDA will seek to ensure the sponsor of a breakthrough therapy product candidate receives: (i) intensive guidance on an efficient drug development program; (ii) intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review; and (iii) a rolling review process whereby FDA may consider reviewing portions of a BLA before the sponsor submits the complete application. Product candidates designated as breakthrough therapies by FDA may be eligible for priority review if supported by clinical data.

Designation as a breakthrough therapy is within the discretion of FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, FDA may disagree. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and, in any event, does not assure ultimate approval by FDA. In addition, even though voretigene neparvovec and SPK-9001 have been designated as breakthrough therapy product candidates, FDA may later decide that one or both no longer meet the conditions for designation or decide that the time period for FDA review or approval will not be shortened.

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

We cannot commercialize a product candidate until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates meet their safety and efficacy endpoints in clinical trials, the regulatory authorities 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

Table of Contents

future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials and the review process.

Regulatory authorities also may approve a product candidate for more limited indications than requested (such as approving voretigene neparvovec for the treatment of patients diagnosed with LCA due to RPE65 mutations but not for the treatment of patients with RP due to RPE65 mutations or other RPE65-mediated IRDs) or they may impose significant limitations in the form of narrow indications, warnings or a REMS. These regulatory authorities may require precautions or contra-indications with respect to conditions of use or they may grant approval subject to the performance of costly post-marketing clinical trials. In addition, regulatory authorities 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 and materially and adversely affect our business, financial condition, results of operations and prospects.

Further, the regulatory authorities may require concurrent approval or the CE mark of a companion diagnostic device. For the product candidates we currently are developing, we believe that diagnoses based on symptoms, in conjunction with existing genetic tests developed and administered by laboratories certified under the Clinical Laboratory Improvement Amendments, or CLIA, are sufficient to diagnose patients and will be permitted by FDA. For future product candidates, however, it may be necessary to use FDA-cleared or FDA-approved diagnostic tests to diagnose patients or to assure the safe and effective use of product candidates in trial subjects. FDA refers to such tests as in vitro companion diagnostic devices. On July 31, 2014, FDA announced the publication of a final guidance document describing the agency's current thinking about the development and regulation of in vitro companion diagnostic devices. The final guidance articulates a policy position that, when safe and effective use of a therapeutic product depends on a diagnostic device, FDA generally will require approval or clearance of the diagnostic device at the same time that FDA approves the therapeutic product. The final guidance allows for two exceptions to the general rule of concurrent drug/device approval, namely, when the therapeutic product is intended to treat serious and life-threatening conditions for which no alternative exists, and when a serious safety issue arises for an approved therapeutic agent, and no FDA-cleared or FDA-approved companion diagnostic test is yet available. At this point, it is unclear how FDA will apply this policy to our current or future gene therapy product candidates. Should FDA deem genetic tests used for diagnosing patients for our therapies to be in vitro companion diagnostics requiring FDA clearance or approval, we may face significant delays or obstacles in obtaining approval of a BLA for our product candidates. In the European Union, the European Commission has proposed substantial revisions to the current regulations governing in vitro diagnostic medical devices. If adopted in their current form, these revisions may impose additional obligations on us that may impact the development and authorization of our product candidates in the EU.

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

Even if we obtain any regulatory approval 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 also may be subject to a REMS, 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 quality, 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, and each of our clinical trials for voretigene neparvovec, SPK-CHM and SPK-9001 includes a 15-year long-term follow-up phase. The holder of an approved BLA also must 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 FDA and other regulatory authorities for compliance with current good manufacturing practices, or cGMP, requirements and adherence to commitments made in the BLA or foreign marketing application.

If we, or a regulatory authority, discover 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 authority 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.

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

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose administrative, civil or criminal penalties or monetary fines;

Table of Contents

- 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 the product or otherwise require the withdrawal of the 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 adversely affect our business, financial condition, results of operations and prospects.

In addition, FDA's policies, and those of equivalent foreign regulatory agencies, 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 materially and adversely affect our business, financial condition, results of operations and prospects.

We face significant competition in an environment of rapid technological change and the possibility that our competitors may achieve regulatory approval before us or develop therapies that are more advanced or effective than ours, which may adversely affect our financial condition and our ability to successfully market or commercialize our product candidates.

The biotechnology and pharmaceutical industries, including the gene therapy field, are characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. We face substantial competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions.

We are aware of companies focused on developing gene therapies in various indications, including Abeona Therapeutics Inc., Adverum Biotechnologies, Inc., Applied Genetic Technologies Corporation, Asklepios BioPharmaceutical Inc., Audentes Therapeutics, Inc., AveXis, Inc., bluebird bio, Inc., Dimension Therapeutics, Inc., Freeline Therapeutics, GenSight Biologics S.A., Horama SAS, Lysogene SAS, MeiraGTx Limited, NightstaRx Ltd., REGENEXBIO Inc., uniQure N.V. and Voyager Therapeutics, Inc., as well as several companies addressing other methods for modifying genes and regulating gene expression. Any advances in gene therapy technology made by a competitor may be used to develop therapies that could compete against any of our product candidates.

For our particular programs, the main competitors include:

- Voretigene neparvovec. While no approved pharmacologic agents exist for patients with RPE65-mediated IRDs, Second Sight Medical Products, Inc. has received approval from FDA and other foreign regulatory authorities for a retinal prosthesis medical device, which is being marketed to RP patients with limited or no light perception. Another retinal prosthesis medical device from Retina Implant AG has obtained a CE Certificate of Conformity from its notified body, and is similarly indicated for blinded RP patients. QLT Inc. completed a Phase 1b clinical trial of a vitamin A derivative to treat RP and LCA. In the gene therapy space, certain companies and several academic institutions have conducted or plan to conduct clinical trials involving RPE65-based product candidates. To date, none of these organizations has completed a trial involving injection of a subject's second eye or has initiated a Phase 3 trial.
- SPK-CHM. We are aware that NightstaRx Ltd. is developing an AAV-based gene therapy for the treatment of choroideremia. NightstaRx Ltd. has been granted orphan product designation by the European Commission and FDA for this product candidate for the treatment of choroideremia and is conducting a Phase 1/2 trial.
- SPK-FIX. Hemophilia B patients typically are treated by a variety of plasma-derived, recombinant or long-acting products that are produced by a number of companies, including Pfizer. Many other companies are developing gene

therapies to treat hemophilia B, including Shire, PLC, Dimension Therapeutics, Inc., Sangamo BioSciences, Inc., Freeline Therapeutics and uniQure N.V.

Table of Contents

- SPK-FVIII. The only therapies currently available for moderate to severe hemophilia A are intravenously administered FVIII protein or its derivatives. The main competitors with product candidates under development to treat hemophilia A include BioMarin Pharmaceutical Inc., Dimension Therapeutics Inc. in collaboration with Bayer HealthCare, uniQure N.V., Sangamo Biosciences, Inc., Telethon Institute for Gene Therapy in collaboration with Biogen Inc., Alnylam Incorporated, Novo Nordisk A/S and Roche Holding AG.
- SPK-TPP1. While there are currently no approved curative therapies for Batten disease, there are a number of companies and academic centers developing enzyme replacement, cell and gene therapies for TPP1 deficiency, including BioMarin Pharmaceuticals Inc., StemCells, Inc. and the Weill Medical College of Cornell University.

Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and other resources, such as larger research and development, clinical, marketing and manufacturing organizations. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of competitors. Our commercial opportunity could be reduced or eliminated if 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. Competitors also may obtain FDA or other regulatory approval for their products more rapidly or earlier 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. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors.

In addition, as a result of the expiration or successful challenge of our patent rights, we could face more litigation with respect to the validity and/or scope of patents relating to our competitors' products. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

Even if we obtain and maintain approval for our product candidates from 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 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 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 FDA grants marketing approval for a product candidate, comparable regulatory authorities of foreign countries also must 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 more onerous 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 EMA for approval of our product candidates in the European Union, but obtaining such approval from the European Commission following the opinion of EMA is a lengthy and expensive process. Even if a product candidate is approved, FDA or the European Commission, 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 additional clinical trials or reporting as conditions of approval. Regulatory authorities in countries outside of the United States and the European Union 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.

Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Also, regulatory approval for any of our product candidates may be withdrawn. If we fail to comply with the regulatory requirements, 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, financial condition, results of operations and prospects will be adversely

affected.

Risks related to third parties

We have in the past entered, and in the future may enter, into collaborations with third parties to develop product candidates. If these collaborations are not successful, our business could be adversely affected.

We have entered into licensing and collaboration agreements with third parties, including our collaboration agreement with Pfizer for the development and commercialization of SPK-FIX product candidates and may enter into additional collaborations in the future. We have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our and our collaborators' abilities to successfully perform the functions assigned to each of us in these

Table of Contents

arrangements. In addition, our collaborators have the ability to abandon research or development projects and terminate applicable agreements. Moreover, an unsuccessful outcome in any clinical trial for which our collaborator is responsible could be harmful to the public perception and prospects of our gene therapy platform.

Our global collaboration agreement with Pfizer, into which we entered in December 2014, as amended in June 2016, relates to the development and commercialization of product candidates for the treatment of hemophilia B. Under this collaboration, we maintain responsibility for clinical development through the completion of Phase 1/2 trials. Thereafter, Pfizer has responsibility for further clinical development, seeking regulatory approvals and commercialization.

We may potentially enter into additional collaborations with third parties in the future. Our relationships with collaborators, including Pfizer, and any future collaborations we enter into in the future, may pose several risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- we may not achieve any milestones, or receive any milestone payments, under our collaborations, including milestones and/or payments that we expect to achieve or receive;
- the clinical trials conducted as part of these collaborations may not be successful;
- 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 clinical trials, 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;
- we may not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our stockholders about the status of such product candidates;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our 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 developed 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, may cause delays or termination of the research, development or commercialization of such product candidates, may lead to additional responsibilities for us with respect to such product candidates or may 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;
- disputes may arise with respect to the ownership of intellectual property developed pursuant to our collaborations;
- 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

Table of Contents

product candidates could be delayed and we may need additional resources to develop our product candidates. In addition, if one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, regulatory approval and commercialization described in this "Risk Factors" section apply to the activities of our collaborators.

We may in the future decide to collaborate with pharmaceutical and biotechnology companies for the 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 several factors. If we license rights to 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 may not be successful in finding strategic collaborators for continuing development of certain of our product candidates or successfully commercializing or competing in the market for certain indications.

We may seek to develop strategic partnerships for developing certain of our product candidates, due to capital costs required to develop the product candidates or manufacturing constraints. We may not be successful in our efforts to establish such 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 or third parties may not view our product candidates as having the requisite potential to demonstrate safety and efficacy. In addition, we may be restricted under existing collaboration agreements from entering into future agreements with potential collaborators. For example, under our collaboration with Pfizer, we are subject to certain restrictions on our ability to directly or indirectly engage in certain activities relating to competing Factor IX gene therapy products. We cannot be certain that, following a strategic transaction or license, we will achieve an economic benefit 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, delay its potential commercialization, 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 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 and our business, financial condition, results of operations and prospects may be materially and adversely affected.

Risks related to manufacturing

Gene therapies are novel, complex and difficult to manufacture. We could experience production problems that result in delays in our development or commercialization programs or otherwise adversely affect our business.

We recently completed construction of our own manufacturing facility, and we may encounter difficulties in validating and operating this new facility. The manufacturing process we use to produce our product candidates is complex, novel and has not been validated for commercial use. Several factors could cause production interruptions, including equipment malfunctions, facility contamination, raw material shortages or contamination, natural disasters, disruption in utility services, human error or disruptions in the operations of our suppliers.

Our product candidates require processing steps that are more complex than those required for most chemical pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as ours generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product will perform in the intended manner. Accordingly, we employ multiple steps to control our manufacturing process to assure that the product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process, could result in

product defects or manufacturing failures that result in lot failures, product recalls, product liability claims or insufficient inventory. We may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

In addition, FDA, EMA and other foreign regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, FDA, EMA or other foreign regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in

Table of Contents

unacceptable changes in the product that could result in lot failures or product recalls. We have experienced lot failures in the past and there is no assurance we will not experience such failures in the future. Lot failures or product recalls could cause us to delay product launches or clinical trials, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects.

We also may encounter problems hiring and retaining the experienced specialist scientific, quality control and manufacturing personnel needed to operate our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements.

Any problems in our manufacturing process or facilities could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs. Problems in our manufacturing process or facilities also could restrict our ability to meet market demand for our products.

Delays in obtaining regulatory approval of our manufacturing process and facility or disruptions in our manufacturing process may delay or disrupt our commercialization efforts. To date, no cGMP gene therapy manufacturing facility in the United States has received approval from FDA for the manufacture of an approved gene therapy product.

Before we can begin to commercially manufacture our product candidates in our own facility, we must obtain regulatory approval from FDA for our manufacturing process and facility. A manufacturing authorization must also be obtained from the appropriate European Union regulatory authorities. To date, no cGMP gene therapy manufacturing facility in the United States has received approval from FDA for the manufacture of an approved gene therapy product and, therefore, the timeframe required for us to obtain such approval is uncertain. In addition, we must pass a pre-approval inspection of our manufacturing facility by FDA before any of our product candidates can obtain marketing approval. In order to obtain approval, we will need to ensure that all of our processes, methods and equipment are compliant with cGMP, and perform extensive audits of vendors, contract laboratories and suppliers. If any of our vendors, contract laboratories or suppliers is found to be out of compliance with cGMP, we may experience delays or disruptions in manufacturing while we work with these third parties to remedy the violation or while we work to identify suitable replacement vendors. The cGMP requirements govern quality control of the manufacturing process and documentation policies and procedures. In complying with cGMP, we will be obligated to expend time, money and effort in production, record keeping and quality control to assure that the product meets applicable specifications and other requirements. If we fail to comply with these requirements, we would be subject to possible regulatory action and may not be permitted to sell any products that we may develop.

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

We currently rely, and expect to continue to rely to a significant degree, on CHOP for the production of our clinical trial materials and, therefore, we can control only certain aspects of their activities. We currently have a manufacturing agreement with CHOP, which we recently amended to provide for continued production of product candidates for our current and future early stage clinical trials. Under certain circumstances, CHOP is entitled to terminate its engagement with us. If we need to enter into alternative arrangements, it could delay our product development activities. Our reliance on CHOP for certain manufacturing activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations. If CHOP does not successfully carry out its contractual duties, meet expected deadlines or manufacture our product candidates in accordance with regulatory requirements, or if there are disagreements between us and CHOP, we will not be able to complete, or may be delayed in completing, the preclinical studies required to support future IND submissions and the clinical trials required for approval of our product candidates. In such instances, 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 or increased expense prior 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 to CHOP, we rely on additional third parties to manufacture ingredients of our product candidates and to perform quality testing, and reliance on these third parties entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- reduced control for certain aspects of manufacturing activities;

- termination or nonrenewal of manufacturing and service 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 and service providers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or service provider.

Table of Contents

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.

Failure to comply with ongoing regulatory requirements could cause us to suspend production or put in place costly or time-consuming remedial measures.

The regulatory authorities may, at any time following approval of a product for sale, audit the manufacturing facilities for such product. If any such inspection or audit identifies a failure to comply with applicable regulations, or if a violation of product specifications or applicable regulations occurs independent of such an inspection or audit, the relevant regulatory authority may require remedial measures that may be costly or time-consuming 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 CHOP or us could materially harm our business, financial condition, results of operations and prospects.

If CHOP or we fail to comply with applicable cGMP regulations, FDA and foreign regulatory authorities can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new product candidate or suspension or revocation of a pre-existing approval. Such an occurrence may cause our business, financial condition, results of operations and prospects to be materially harmed.

Additionally, if supply from CHOP or from our facility 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 supplement to its regulatory filing, which could result in further delay. The regulatory authorities also may require additional trials if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and could result in a delay in our desired clinical and commercial timelines.

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 currently rely on CHOP and other third parties to manufacture certain of our product candidates and to perform quality testing, and because we collaborate with various organizations and academic institutions for the advancement of our gene therapy platform, we must, at times, share our proprietary technology and confidential information, including 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. 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 proprietary technology and confidential information or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business, financial condition, results of operations and prospects.

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 by third parties. A competitor’s discovery of our trade secrets would impair our competitive position and have an adverse impact on our business, financial condition, results of operations and prospects.

Any contamination in our manufacturing process, shortages of raw materials or failure of any of our key suppliers to deliver necessary components could result in delays in our clinical development or marketing schedules.

Given the nature of biologics manufacturing, there is a risk of contamination. Any contamination could materially adversely affect our ability to produce product candidates on schedule and could, therefore, harm our results of operations and cause reputational damage.

Some of the raw materials required in our manufacturing process are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination,

recall or restriction on the use of biologically derived substances in the manufacture of our product candidates could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could materially and adversely affect our development timelines and our business, financial condition, results of operations and prospects.

Table of Contents

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 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. 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 be 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 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 business, financial condition, results of operations and prospects.

Risks related to the commercialization of our product candidates

If we are unable to expand our sales, medical affairs and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any product revenue.

We currently have a small sales and marketing organization. To successfully commercialize any products that may result from our development programs, we will need to expand these capabilities, either on our own or with others. The development of our own commercial team 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 have entered into a collaboration with Pfizer for the development and commercialization of SPK-FIX product candidates for the treatment of hemophilia B pursuant to which Pfizer would commercialize such product candidates, and we would be eligible to receive specified milestone payments and royalties, for any product developed under the agreement. We may enter into collaborations regarding other of our product candidates with other entities to utilize their established marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If any current or future collaborators do not commit sufficient resources to commercialize our products, or we are unable to develop the necessary capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business.

We compete with many companies that currently have extensive, experienced and well-funded medical affairs, 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.

As part of our plan to market voretigene neparvovec through a limited number of centers that specialize in treating IRDs, we will need to train additional vitreoretinal surgeons to perform the procedure necessary to administer voretigene neparvovec to patients safely and effectively via sub-retinal injection. This procedure requires significant skill and training. If we are unable to recruit or train sufficient retinal surgeons to perform the procedure properly, the availability of voretigene neparvovec could be substantially diminished, which would adversely affect our business, financial condition, results of operations and prospects.

Our efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may never be successful. Such efforts may require more resources than are typically required due to the complexity and uniqueness of our potential products. If any of our product candidates is approved but fails to achieve market acceptance among physicians, patients or third-party payors, we will not be able to generate significant revenues from such product, which could have a material adverse effect on our business, financial

condition, results of operations and prospects.

If the market opportunities for our product candidates are smaller than we believe they are, our product revenues may be adversely affected and our business may suffer.

We focus our research and product development on treatments for severe genetic and orphan diseases. Our understanding of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. These estimates may prove to be incorrect and new studies may reduce the estimated incidence or prevalence of these diseases. The number of patients in the United States, the European Union and elsewhere may turn out to be lower than expected, may not be otherwise amenable to

Table of Contents

treatment with our products or patients may become increasingly difficult to identify and access, all of which would adversely affect our business, financial condition, results of operations and prospects.

Further, there are several factors that could contribute to making the actual number of patients who receive our potential products less than the potentially addressable market. These include the lack of widespread availability of, and limited reimbursement for, new therapies in many underdeveloped markets. Further, the severity of the progression of a disease up to the time of treatment, especially in certain degenerative conditions such as IRDs caused by mutations in the RPE65 gene, will likely diminish the therapeutic benefit conferred by a gene therapy due to irreversible cell death. Lastly, certain patients' immune systems might prohibit the successful delivery of certain gene therapy products to the target tissue, thereby limiting the treatment outcomes.

The insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our products, if approved, could limit our ability to market those products and decrease our ability to generate product 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 government 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 will be reimbursed by government authorities, private health coverage insurers and other third-party payors. Coverage and reimbursement by a third-party payor may depend upon several 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 for a product from third-party payors is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-effectiveness data. 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 are available only at 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 adequate 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 government 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 government payors develop their coverage and reimbursement policies. Currently, no gene therapy product has been approved for coverage and reimbursement by the Centers for Medicare & Medicaid Services, or CMS, the agency responsible for administering the Medicare program. 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 types of products. Moreover, reimbursement agencies in the European Union may be more conservative than CMS. For example, several cancer drugs have been approved for reimbursement in the United States and have not been approved for reimbursement in certain European Union Member States. It is difficult to predict what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

Outside the United States, international operations generally are subject to extensive government price controls and other market regulations, and increasing emphasis on cost-containment initiatives in the European Union, Canada and other countries may put pricing pressure on us. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. It also can take a significant amount of time after approval of a product to secure pricing and reimbursement for such product in many counties outside the United States. 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 product revenues.

Table of Contents

Moreover, increasing efforts by government 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. Payors increasingly are considering new metrics as the basis for reimbursement rates, such as average sales price, or ASP, average manufacturer price, or AMP, and Actual Acquisition Cost. The existing data for reimbursement based on some of these metrics is relatively limited, although certain states have begun to survey acquisition cost data for the purpose of setting Medicaid reimbursement rates, and CMS has begun making pharmacy National Average Drug Acquisition Cost and National Average Retail Price data publicly available on at least a monthly basis. Therefore, it may be difficult to project the impact of these evolving reimbursement metrics on the willingness of payors to cover candidate products that we or our partners are able to commercialize. 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 intense. As a result, increasingly high barriers are being erected to the entry of new products such as ours.

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 could result in additional regulations restricting or prohibiting our products. Even with the requisite approvals from FDA in the United States, EMA in the European Union and other regulatory authorities internationally, the commercial success of our product candidates will depend, in part, on the acceptance of physicians, patients and health care payors of gene therapy products in general, and our product candidates in particular, as medically necessary, cost-effective and safe. Any product that we commercialize may not gain acceptance by physicians, patients, health care 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 gene therapy products and, in particular, our product candidates, if approved for commercial sale, will depend on several 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 cost of treatment relative to alternative treatments;
- the clinical indications for which the product candidate is approved by FDA or the European Commission;
- patient awareness of, and willingness to seek, genotyping;
- the willingness of physicians to prescribe new therapies;
- the willingness of the target patient population to try new therapies;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of FDA, EMA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- relative convenience and ease of administration;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments; and
- sufficient third-party payor 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.

Table of Contents

Our gene therapy approach utilizes vectors derived from viruses, which may be perceived as unsafe or may result in unforeseen adverse events. Negative public opinion and increased regulatory scrutiny of gene therapy may damage public perception of the safety of our product candidates and 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 for a genetic disease to date in the United States and only one gene therapy product for a genetic disease approved to date in the European Union. 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 who specialize in the treatment of genetic diseases targeted by our product candidates, prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments with which they are familiar and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have an adverse effect on our business, financial condition, results of operations and prospects and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. For example, earlier gene therapy trials led to several well-publicized adverse events, including cases of leukemia and death seen in other trials using other vectors. Serious adverse events in our clinical trials, or other clinical trials involving gene therapy products or our competitors' products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity, could result in increased government 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.

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

We expect that we will be subject to additional risks in commercializing our product candidates outside the United States, including:

- different regulatory requirements for approval of drugs and biologics in foreign countries;
- reduced protection for intellectual property rights;
- 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;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- 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.

Risks related to our business operations

We may not be successful in our efforts to identify or discover additional product candidates and may fail to capitalize on programs or product candidates that may be a greater commercial opportunity or for which there is a greater likelihood of success.

The success of our business depends upon our ability to identify, develop and commercialize product candidates based on our gene therapy platform. Research programs to identify new product candidates require substantial technical, financial and human resources. 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 several reasons. For example, our research may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects, may be commercially impracticable to manufacture or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval. Additionally, 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 spending

on current and future research and development programs may not yield any commercially viable products. If we do not accurately evaluate the commercial potential for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other arrangements in cases in which it would have been more advantageous for us to retain

Table of Contents

sole development and commercialization rights to such product candidate. Alternatively, 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.

If any of these events occur, we may be forced to abandon our development efforts with respect to a particular product candidate or fail to develop a potentially successful product candidate, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

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 members of our executive team, the loss of whose services may adversely impact the achievement of our objectives. While we have entered into employment agreements with each of our executive officers, any of them could leave our employment at any time, as all of our employees are "at will" employees. We do not have "key person" insurance on any of our employees. The loss of the services of one or more of our current employees might impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel, also will be critical to our success. There currently is a shortage of skilled individuals with substantial gene therapy experience, which is likely to continue. As a result, competition for skilled personnel, including in gene therapy research and vector manufacturing, 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 and academic institutions for individuals with similar skill sets. In addition, failure to succeed in preclinical or clinical trials or applications for marketing approval may make it more challenging to recruit and retain qualified personnel. The inability to recruit, or loss of services of certain executives, key employees, consultants or advisors, may impede the progress of our research, development and commercialization objectives and have a material adverse effect on our business, financial condition, results of operations and prospects.

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 commercial infrastructure to support commercialization of any of our product candidates that are approved for sale. Future growth would impose significant added responsibilities on members of management. It is likely 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 product candidates 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 employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the European Union and other jurisdictions, provide accurate information to FDA, the European Commission and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose 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 restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with FDA or other regulatory authorities, 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 government 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, financial condition, results of operations and prospects, including the imposition of significant fines or other sanctions.

Table of Contents

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, several 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 the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. The PPACA, among other things: (i) 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; (ii) 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; (iii) establishes annual fees and taxes on manufacturers of certain branded prescription drugs; (iv) expands the availability of lower pricing under the 340B drug pricing program by adding new entities to the program; and (v) 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. Additionally, in the United States, the Biologics Price Competition and Innovation Act of 2009 created an abbreviated approval pathway for biologic products that are demonstrated to be "highly similar" or "biosimilar or interchangeable" with an FDA-approved biologic product. This new pathway could allow competitors to reference data from biologic products already approved after 12 years from the time of approval. This could expose us to potential competition by lower-cost biosimilars even if we commercialize a product candidate faster than our competitors.

Additional changes that may affect our business include those governing enrollment in federal healthcare programs, reimbursement changes, rules regarding prescription drug benefits under the health insurance exchanges and fraud and abuse and enforcement. Continued implementation of the PPACA and the passage of additional laws and regulations may result in the expansion of new programs such as Medicare payment for performance initiatives, and may impact existing government healthcare programs, such as by improving the physician quality reporting system and feedback program.

For each state that does not choose to expand its Medicaid program, there likely will be fewer insured patients overall, which could impact the sales, business and financial condition of manufacturers of branded prescription drugs. Where patients receive insurance coverage under any of the new options made available through the PPACA, the possibility exists that manufacturers may be required to pay Medicaid rebates on that resulting drug utilization, a decision that could impact manufacturer revenues. The U.S. federal government also has announced delays in the implementation of key provisions of the PPACA. The implications of these delays for our and our partners' business and financial condition, if any, are not yet clear.

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.

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 will be directly, or indirectly through our prescribers, customers and purchasers, subject to various federal and state fraud and abuse laws and regulations, including, without limitation, the federal Health Care Program Anti-Kickback Statute, the federal civil and criminal False Claims Act and Physician Payments Sunshine Act and regulations. These laws will 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 will affect our operations 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. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers and formulary managers on the other. The PPACA amends the intent requirement of the federal Anti-Kickback Statute. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it;

- 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 payors that are false or fraudulent. The PPACA provides and recent government cases against pharmaceutical and medical device manufacturers support the view that Federal Anti-

Table of Contents

Kickback Statute violations and certain marketing practices, including off-label promotion, may implicate the False Claims Act;

- 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;
- federal transparency laws, including the federal Physician Payment Sunshine Act, that require 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; and
- state law equivalents of each of the above federal laws, 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. If our operations are found to be in violation of any of the laws described above or any other government 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.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the European Union. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of European Union Member States, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain European Union Member States must be publically disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

The collection and use of personal health data in the European Union, presently governed by the provisions of the Data Protection Directive will be replaced with the General Data Protection Regulation, or GDPR, which is currently going through the adoption process. The GDPR will impose several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, the security and confidentiality of the personal data, data breach notification and using third party processors in connection with the processing of the personal data. The GDPR will also impose strict rules on the transfer of personal data out of the European Union to the United States. Failure to comply with the requirements of the GDPR and the applicable national data protection laws of the European Union Member States may result in fines and other administrative penalties. The GDPR will introduce substantial fines for breaches of the data protection rules. It is expected to be formally adopted in 2016 and to become enforceable in 2018. Once it is enforceable, the GDPR may increase our

responsibility and liability in relation to personal data that we process. To comply with the new data protection rules imposed by the GDPR we may be required to put in place additional mechanisms ensuring compliance. This may be onerous and adversely affect our business, financial condition, results of operations and prospects.

Table of Contents

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any product candidates that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in clinical trials and may face an even greater risk if we commercialize any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

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

Although we maintain product liability insurance coverage, this insurance may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage each time we commence a clinical trial and if we successfully commercialize any product candidate. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

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 generation, handling, use, storage, treatment, manufacture, transportation and disposal of, and exposure to, hazardous materials and wastes, as well as laws and regulations relating to occupational health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biologic and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. 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 for certain 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. We do not maintain insurance for toxic tort claims that may be asserted against us in connection with our storage or disposal of biologic, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations, which have tended to become more stringent over time. 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 or liabilities, which could materially adversely affect our business, financial condition, results of operations and prospects.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The most recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the most recent global financial crisis, could result in a variety of risks to our business, including weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. This is particularly true in the European Union, which is undergoing a continued severe economic crisis. A weak or declining economy could strain our suppliers, possibly resulting in supply disruption, or cause delays in payments for our services by third-party payors or our collaborators. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

48

Table of Contents

Third parties on which we rely and we may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters could severely disrupt our operations or the operations of CHOP's manufacturing facilities and have a material adverse effect on our business, financial condition, results of operations and prospects. 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, such as CHOP's manufacturing facilities, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and may not prove adequate in the event of a serious disaster or similar event. Both CHOP's manufacturing facility and our manufacturing facility, as well as substantially all of our current supply of product candidates, are located in Philadelphia, Pennsylvania, and we do not have any existing back-up facilities in place or plans for such back-up facilities. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, accident or security breach to date, 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, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

Risks related to our intellectual property

Our rights to develop and commercialize our product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.

We are heavily reliant upon licenses to certain patent rights and proprietary technology from third parties that are important or necessary to the development of our technology and products, including technology related to our manufacturing process and our gene therapy product candidates. These and other licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future. As a result, we may not be able to prevent competitors from developing and commercializing competitive products in territories included in all of our licenses.

Licenses to additional third-party technology that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, or at all, which could have a material adverse effect on our business and financial condition.

In some circumstances, we may 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. For example, pursuant to each of our intellectual property licenses with CHOP, Penn and the University of Iowa Research Foundation, or UIRF, our licensors retain control of such activities. Therefore, we cannot be certain that these patents and applications will be prosecuted, maintained and enforced in a manner consistent with the best interests of our business. If our licensors fail to maintain such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected. In addition to the foregoing, the risks associated with patent rights that we license from third parties will also apply to patent rights we may own in the future.

49

Table of Contents

Furthermore, the research resulting in certain of our licensed patent rights and technology was funded by the U.S. government. As a result, the government may have certain rights, or march-in rights, to such patent rights and technology. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a non-exclusive license authorizing the government to use the invention for non-commercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use our licensed technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government of such rights could harm our competitive position, business, financial condition, results of operations and prospects.

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

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 product candidates and manufacturing technology. Our licensors have sought and we intend to seek to protect our proprietary position by filing patent applications in the United States and abroad related to many of our novel technologies and product candidates that are important to our business.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain, enforce or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, certain patents in the field of gene therapy that may have otherwise potentially provided patent protection for certain of our product candidates have expired or will soon expire. In some cases, the work of certain academic researchers in the gene therapy field has entered the public domain, which we believe precludes our ability to obtain patent protection for certain inventions relating to such work. As a result, we have not sought, and may be unable to seek, patent protection for SPK-CHM to treat choroideremia or for voretigene neparvovec to treat RPE65-mediated IRDs other than LCA. Consequently, we will not be able to assert any such patents to prevent others from using our technology for, and developing and marketing competing products to treat, these indications. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

We are a party to intellectual property license agreements with CHOP, Penn and UIRF, each of which is important to our business, as well as license agreements with Clearside, 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, development and commercialization timelines, milestone payments, royalties 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.

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. 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 patents being issued which protect our technology or product candidates or which effectively prevent others from commercializing competitive technologies and product candidates. 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.

We may not be aware of all third-party intellectual property rights potentially relating to our product candidates. Publications of discoveries in the scientific literature often lag the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in any owned or any

licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

Even if the patent applications we license or may own in the future do issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us or otherwise provide us with any competitive advantage. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

Table of Contents

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our 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 in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. 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 intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Our intellectual property licenses with third parties may be subject to disagreements over contract interpretation, which could narrow the scope of our rights to the relevant intellectual property or technology or increase our financial or other obligations to our licensors.

The agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

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.

We have entered into license agreements with third parties and may need to obtain additional licenses from others to advance our research or allow commercialization of our product candidates. It is possible that we may be unable to obtain additional 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 redesign our product candidates or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. 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 manufacturing methods, product candidates or future methods or products, resulting in either an injunction prohibiting our manufacture or 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 each of our existing license agreements, and we expect in our future agreements, patent prosecution of our licensed technology is controlled solely by the licensor, and we are required to reimburse the licensor for their costs of patent prosecution. 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. Further, in each of our license agreements we are responsible for bringing any actions against any third party for infringing on the patents we have licensed. Certain of our license agreements also require us to meet development thresholds to maintain the license, including establishing a set timeline for developing and commercializing products and minimum yearly diligence obligations in developing and commercializing the product. 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 inventorship or 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.

Table of Contents

We may not be successful in obtaining necessary rights to our product candidates through acquisitions and in-licenses. We currently have rights to the intellectual property, through licenses from third parties, to develop our product candidates. Because our programs may require the use of proprietary rights held by third parties, the growth of our business likely will depend, in part, on our ability to acquire, in-license or use these proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes or other intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue 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, capital resources and greater clinical development and commercialization capabilities. 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.

We sometimes collaborate with non-profit and 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 option, we may be unable to negotiate a license within the specified timeframe 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.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate and our business, financial condition, results of operations and prospects could suffer.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by government 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 government fees on patents and/or applications will be due to be paid to the United States Patent and Trademark Office, or USPTO, and various government patent agencies outside of the United States over the lifetime of our licensed patents and/or applications and any patent rights we may own in the future. We rely on our outside counsel or our licensing partners to pay these fees due to non-U.S. patent agencies. The USPTO and various non-U.S. government patent agencies require compliance with several 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 we are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. 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. There are situations, however, 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.

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 could be less extensive than those in the United States. Although our license agreements with CHOP, Penn and UIRF grant us worldwide rights, certain of our in-licensed U.S. patent rights lack corresponding foreign patents or patent applications. For example, we license a U.S. patent from Penn that covers methods of treating patients with LCA due to RPE65 mutations. No patents or patent applications outside the United States corresponding to this patent were ever pursued. 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, 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.

Table of Contents

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.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court. We may not be able to protect our trade secrets in court.

If one of our licensing partners or we 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, written description or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld information material to patentability from the USPTO, or made a misleading statement, during prosecution. Third parties also may 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, inter partes review and equivalent proceedings in foreign jurisdictions. Such proceedings could result in the revocation or cancellation 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 the patent examiner and we or our licensing partners 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.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect and some courts inside and outside the United States are less willing or unwilling to protect trade secrets. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors.

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

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our

product candidates and technology, including interference proceedings, post grant review and inter partes review before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. We are aware of certain third party patents relating to gene delivery to ocular cells and certain vector manufacturing methods that may relate to, and potentially could be asserted to encompass, our voretigene neparvovec, SPK-CHM, SPK-FIX, SPK-FVIII, and SPK-TPP1 programs. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could materially and adversely affect our ability to commercialize product candidates in our voretigene neparvovec, SPK-CHM, SPK-FIX, SPK-FVIII, and SPK-TPP1 programs or any of our product candidates or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of

Table of Contents

validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. If we are found to infringe a third party's valid and enforceable intellectual property rights, we could be required to obtain a license from such third party to continue developing, manufacturing and marketing our product candidates and technology. However, we may not be able to obtain any required license 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 and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product candidates. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from manufacturing and commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects.

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

Competitors may infringe our patents or the patents of our licensing partners, or we may be required to defend against claims of infringement. To counter infringement or unauthorized use claims or to defend against claims of infringement can be expensive and time consuming. 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 adequately conduct such litigation or proceedings. 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 and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Many of our employees, consultants or advisors are currently, or 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 advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. 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. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of 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 several significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and also may affect patent litigation. These also include provisions that switched the United States from a “first-to-invent” system to a “first-to-file” system, allow third-party submission of prior art to the USPTO during patent prosecution and set forth additional procedures to attack the validity of a patent by the USPTO administered post grant proceedings. Under a first-to-file system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention

Table of Contents

regardless of whether another inventor had made the invention earlier. The USPTO 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, financial condition, results of operations and prospects.

The patent positions of companies engaged in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Two cases involving diagnostic method claims and “gene patents” have recently been decided by the Supreme Court of the United States, or Supreme Court. On March 20, 2012, the Supreme Court issued a decision in Mayo Collaborative Services v. Prometheus Laboratories, Inc., or Prometheus, a case involving patent claims directed to a process of measuring a metabolic product in a patient to optimize a drug dosage for the patient. According to the Supreme Court, the addition of well-understood, routine or conventional activity such as “administering” or “determining” steps was not enough to transform an otherwise patent-ineligible natural phenomenon into patent-eligible subject matter. On July 3, 2012, the USPTO issued a guidance memo to patent examiners indicating that process claims directed to a law of nature, a natural phenomenon or a naturally occurring relation or correlation that do not include additional elements or steps that integrate the natural principle into the claimed invention such that the natural principle is practically applied and the claim amounts to significantly more than the natural principle itself should be rejected as directed to not patent-eligible subject matter. On June 13, 2013, the Supreme Court issued its decision in Association for Molecular Pathology v. Myriad Genetics, Inc., or Myriad, a case involving patent claims held by Myriad Genetics, Inc. relating to the breast cancer susceptibility genes BRCA1 and BRCA2. Myriad held that an isolated segment of naturally occurring DNA, such as the DNA constituting the BRCA1 and BRCA2 genes, is not patent eligible subject matter, but that complementary DNA, which is an artificial construct that may be created from RNA transcripts of genes, may be patent eligible.

On March 4, 2014, the USPTO issued a guidance memorandum to patent examiners entitled "2014 Procedure For Subject Matter Eligibility Analysis Of Claims Reciting Or Involving Laws Of Nature/Natural Principles, Natural Phenomena, And/Or Natural Products." On December 6, 2014, a memorandum entitled "2014 Interim Guidance on Subject Matter Eligibility" was published. On July 30, 2015, an update pertaining to patent subject matter eligibility was published by the USPTO. These guidelines instruct USPTO examiners on the ramifications of the Prometheus and Myriad rulings and apply the Myriad ruling to natural products and principles including all naturally occurring nucleic acids. Patents for certain of our product candidates contain claims related to specific DNA sequences that are naturally occurring and, therefore, could be the subject of future challenges made by third parties. In addition, the recent USPTO guidance could make it impossible for us to pursue similar patent claims in patent applications we may prosecute in the future.

There can be no assurance that our efforts to seek patent protection for our technology and products will not be negatively impacted by the decisions described above, rulings in other cases or changes in guidance or procedures issued by the USPTO. We cannot fully predict what impact the Supreme Court’s decisions in Prometheus and Myriad may have on the ability of life science companies to obtain or enforce patents relating to their products and technologies in the future. These decisions, the guidance issued by the USPTO and rulings in other cases or changes in USPTO guidance or procedures could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

Moreover, although the Supreme Court has held in Myriad that isolated segments of naturally occurring DNA are not patent-eligible subject matter, certain third parties could allege that activities that we may undertake infringe other gene-related patent claims, and we may deem it necessary to defend ourselves against these claims by asserting non-infringement and/or invalidity positions, or paying to obtain a license to these claims. In any of the foregoing or in other situations involving third-party intellectual property rights, if we are unsuccessful in defending against claims of patent infringement, we could be forced to pay damages or be subjected to an injunction that would prevent us from utilizing the patented subject matter. Such outcomes could harm our business, financial condition, results of operations or prospects.

If we do not obtain patent term extension and data exclusivity for our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of

Table of Contents

patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

We have allowed trademark applications with the USPTO for the mark "SPARK" and the Spark logo, however, a valid statement of use must be filed for such applications to issue as registered trademarks. Whether allowed or registered, our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make gene therapy products that are similar to our product candidates but that are not covered by the claims of the patents that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that our pending licensed patent applications or those that we may own in the future will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may have an adverse effect on our business; and
- we may choose not to file a patent for certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could significantly harm our business, financial condition, results of operations and prospects.

Risks related to ownership of our common stock

Our executive officers, directors and principal stockholders maintain the ability to exert substantial influence over matters submitted to stockholders for approval.

As of August 3, 2016, our executive officers, directors and principal stockholders, in the aggregate, beneficially own shares representing approximately 30.8% of our outstanding capital stock. As a result, if these stockholders were to act together, they would be able to exert substantial influence over all matters submitted to our stockholders for

approval, as well as our management and affairs. For example, these persons, if they act together, may control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or

Table of Contents

prevent an acquisition of our company on terms that other stockholders may desire or result in management of our company that our public stockholders disagree with.

A significant number of our total outstanding shares may be sold into the market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is performing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Our outstanding shares of common stock may be freely sold in the public market at any time to the extent permitted by Rules 144 and 701 under the Securities Act of 1933, as amended, or the Securities Act, or to the extent such shares have already been registered under the Securities Act and are held by non-affiliates of ours. Moreover, as of August 3, 2016, holders of a substantial number of shares of our common stock have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. In addition, in connection with our acquisition of Genable, on June 3, 2016 we filed a resale registration statement to register the 265,000 shares of common stock we issued to Genable shareholders as part of the transaction. In January 2015, we filed a registration statement registering all shares of common stock that we may issue under our equity compensation plans. As of August 3, 2016, we had outstanding options to purchase an aggregate of 4,078,000 shares of our common stock, of which options to purchase 1,002,837 were vested. These shares can be freely sold in the public market upon issuance, subject to volume limitations and black-out periods applicable to affiliates.

In addition, certain of our employees, executive officers, directors and affiliated stockholders, including Sofinnova Venture Partners VIII, L.P., have entered or may enter into Rule 10b5-1 plans providing for sales of shares of our common stock from time to time. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the employee, director or officer when entering into the plan, without further direction from the employee, officer, director or affiliated stockholder. A Rule 10b5-1 plan may be amended or terminated in some circumstances. Our employees, executive officers, directors and affiliated stockholders also may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

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

The trading market for our common stock relies, in part, on the research and reports that industry or financial analysts publish about us or our business. Although we have obtained analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock or fail to regularly publish reports on us, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

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

Our stock price is likely to be volatile. The stock market in general, and the market for biopharmaceutical companies in particular, has experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our stockholders may not be able to sell their shares of common stock at or above the price they paid for their shares. The market price for our common stock may be influenced by many factors, including:

- results of clinical trials of our product candidates or those of our competitors;
- the success of competitive products or technologies;
- commencement or termination of collaborations;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates;
-

actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;

- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;

Table of Contents

- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

In the past, following periods of volatility in the market price of a company's securities, securities class-action litigation often has been instituted against that company. Such litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert management's attention and resources, which could seriously harm our business, financial condition, results of operations and prospects.

An active trading market for our common stock may not be sustained.

Our shares of common stock began trading on the NASDAQ Global Select Market on January 30, 2015. Given the limited trading history of our common stock, there is a risk that an active trading market for our shares may not continue to develop or be sustained. If an active market for our common stock does not continue to develop or is not sustained, it may be difficult for our stockholders to sell shares without depressing the market price for the shares, or at all.

We have broad discretion in the use of our cash, cash equivalents and marketable securities and may not use them effectively.

Our management has broad discretion in the application of our cash, cash equivalents and marketable securities and could spend these funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value.

Commencing January 1, 2017 we will no longer be an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies will no longer apply.

We currently are an "emerging growth company," or EGC, as defined in the JOBS Act. As of June 30, 2016, the market value of our common stock that was held by non-affiliates exceeded $700 million and, therefore, we will no longer qualify for such status commencing January 1, 2017. As a large-accelerated filer, we will be subject to certain disclosure requirements that are applicable to other public companies that have not been applicable to us as an emerging growth company, beginning with our Annual Report on Form10-K filed for the fiscal year 2016. These requirements include:

- being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002;
- being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- full disclosure obligations regarding executive compensation; and
- compliance with the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

In addition, we will no longer be able to take advantage of an extended transition period for complying with new or revised accounting standards.

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

As a public company we incur, and particularly commencing January 1, 2017, when we will no longer be an EGC, we will incur further, significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the SEC and NASDAQ have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial

amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and will make some activities more time-consuming and costly.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial

Table of Contents

reporting issued by our independent registered public accounting firm. Commencing January1, 2017, when we will no longer be an EGC, we will be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

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

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions also could limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a shareholder rights plan, or so-called “poison pill,” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

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

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

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

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

Use of Proceeds from Initial Public Offering of Common Stock

On February 4, 2015, we closed our initial public offering of 8,050,000 shares of our common stock, including 1,050,000 shares of our common stock pursuant to the exercise by the underwriters of an option to purchase additional shares, at a public offering price of $23.00 per share for an aggregate offering of approximately $185.2 million. The offer and sale of all of the

Table of Contents

shares in the offering were registered under the Securities Act pursuant to registration statement on Form S-1 (File No. 333-201318), which was declared effective by the SEC on January 29, 2015, and registration statement on Form S-1 MEF (File No. 333-201764) filed pursuant to Rule 462(b) of the Securities Act. J.P. Morgan Securities LLC and Credit Suisse Securities (USA) LLC acted as joint book-running managers for the offering and as representatives of the underwriters. Cowen and Company, LLC acted as lead manager and Sanford C. Bernstein & Co., LLC acted as co-manager. The offering commenced on January 29, 2015 and did not terminate until the sale of all of the shares offered.

There has been no material change in our planned use of the net proceeds from the offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act. As of June 30, 2016, the entire amount of the net proceeds is included as cash and cash equivalents.

Item 5. Other Information

None.

Item 6. Exhibits

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

Table of Contents

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: August 10, 2016

SPARK THERAPEUTICS, INC.

By: /s/ Jeffrey D. Marrazzo
Jeffrey D. Marrazzo
Chief Executive Officer
(Principal Executive Officer)

Table of Contents

EXHIBIT INDEX

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
10.1†	Amendment No. 1, dated June 9, 2016 to the License Agreement dated December 6, 2014 between the Registrant and Pfizer					X
10.2	Form of Employment Agreement for executive officers					X
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended					X
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended					X
32.1	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
32.2	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
101	The following materials from the Company's Quarterly Report on Form10-Q for the quarter ended June 30, 2016, formatted in XBRL (eXtensible Business Reporting Language): (i) Consolidated Balance Sheets as of December 31, 2015 and June 30, 2016, (ii) Consolidated Statements of Operations for the three and six months ended June 30, 2015 and 2016, (iii) Consolidated Statements of Cash Flows for the six months ended June 30, 2015 and 2016 and (v) Notes to Unaudited Consolidated Financial Statements.					X

† Confidential treatment requested as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.