Spark Therapeutics, Inc.
Form 10-Q
August 08, 2018
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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, 2018

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, a smaller reporting company or an emerging growth company. See the definitions of “large accelerated filer”, “accelerated filer”, “smaller reporting company” and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

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

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

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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 1, 2018 there were 37,571,535 shares of the registrant's Common Stock, par value $0.001 per share, outstanding.

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FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical fact, 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:

- our expectations regarding our commercial launch of LUXTURNA™ (voretigene neparvovec-rzyl), which is still in its initial phases, and our plans to develop and commercialize our other product candidates;
- the timing, scope or likelihood of regulatory filings and approvals, including the timing of European Medicines Agency, or EMA, approval, if any, for the marketing authorization application, or MAA, of LUXTURNA;
- our ability to enter into agreements involving outcomes-based rebates and innovative contracting models with payers for LUXTURNA;
- our estimates regarding the potential market opportunity for LUXTURNA and our product candidates;
- the timing, progress and results of clinical trials for SPK-7001, SPK-9001, SPK-8011 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;
- 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 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;
- our expectations about the rate and degree of market acceptance and clinical utility of LUXTURNA and 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 the use of our capital resources;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing; and
- the impact of government laws and regulations.

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 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.

PART I. FINANCIAL INFORMATION

Item 1. Financial Statements

Spark Therapeutics, Inc.
Consolidated balance sheets (unaudited)
(in thousands, except share and per share data)

	December 31, 2017	June 30, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 96,748	$201,086
Marketable securities	423,419	446,141
Trade and other receivables	7,906	25,239
Inventory	—	12,674
Prepaid expenses	5,093	6,414
Total current assets	533,166	691,554
Marketable securities	20,035	9,552
Property and equipment, net	61,713	68,698
Goodwill	1,254	1,223
Other assets	628	2,492
Total assets	$ 616,796	$773,519
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 14,183	$8,785
Accrued expenses	24,697	23,849
Current portion of long-term debt	312	317
Current portion of deferred rent	969	989
Current portion of deferred revenue	11,969	1,841
Current other liabilities	1,557	1,656
Total current liabilities	53,687	37,437
Long-term debt	912	752
Long-term deferred rent	8,318	7,914
Long-term deferred revenue	—	105,000
Other liabilities	40,255	38,676
Total liabilities	103,172	189,779
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; 37,131,626 shares issued and 37,111,404 shares outstanding as of December 31, 2017; 37,543,411 shares issued and 37,476,978 shares outstanding as of June 30, 2018	37	38
Additional paid-in capital	1,026,590	1,065,438
Accumulated other comprehensive loss	(5,914)	(643)
Treasury stock, at cost, 20,222 shares as of December 31, 2017 and 66,433 shares as of June 30, 2018	(1,226)	(4,020)
Accumulated deficit	(505,863)	(477,073)
Total stockholders' equity	513,624	583,740
Total liabilities and stockholders' equity	$ 616,796	$773,519

See accompanying notes to the unaudited consolidated financial statements.

Spark Therapeutics, Inc.
Consolidated statements of operations and comprehensive income (loss)
(unaudited)
(in thousands, except share and per share data)

	Three months ended June 30,		Six months ended June 30,	
	2017	2018	2017	2018
Revenues:				
Product sales, net	$—	$ 4,314	$—	$ 6,733
Contract revenue	1,483	20,871	2,758	34,128
Total revenues	1,483	25,185	2,758	40,861
Operating expenses:				
Cost of product sales	—	269	—	390
Cost of contract revenue	—	4,242	—	5,111
Research and development	32,989	25,524	65,338	55,633
Acquired in-process research and development	3,070	—	3,457	—
Impairment of acquired in-process research and development	15,696	—	15,696	—
Selling, general and administrative	26,729	29,749	48,142	63,238
Total operating expenses	78,484	59,784	132,633	124,372
Loss from operations	(77,001)	(34,599)	(129,875)	(83,511)
Unrealized gain on equity investments	—	2,255	—	2,619
Interest income, net	532	2,521	1,117	4,706
Other income	—	110,000	—	110,000
Income (loss) before income taxes	(76,469)	80,177	(128,758)	33,814
Income tax benefit (expense)	2,109	(12)	2,109	(22)
Net income (loss)	$(74,360)	$ 80,165	$(126,649)	$ 33,792
Basic net income (loss) per common share	$(2.40)	$ 2.15	$(4.10)	$ 0.91
Diluted net income (loss) per common share	$(2.40)	$ 2.07	$(4.10)	$ 0.88
Weighted average basic common shares outstanding	30,968,450	37,254,003	30,870,740	37,150,693
Weighted average diluted common shares outstanding	30,968,450	38,702,598	30,870,740	38,385,097
Net income (loss)	$(74,360)	$ 80,165	$(126,649)	$ 33,792
Other comprehensive income (loss):				
Unrealized gain on available-for-sale securities, net of tax	1,644	470	1,343	306
Foreign exchange translation adjustment	697	(58)	102	(37)
Total comprehensive income (loss)	$(72,019)	$ 80,577	$(125,204)	$ 34,061

See accompanying notes to the unaudited consolidated financial statements.

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

	Six months ended June 30,	
	2017	2018
Cash flows from operating activities:		
Net income (loss)	$(126,649)	$33,792
Adjustments to reconcile net income (loss) to net cash (used in) provided by operating activities:		
Non-cash rent expense (income)	534	(1,118)
Depreciation and amortization expense	2,226	3,125
Loss on disposal of property and equipment	—	59
Acquired in-process research and development	3,457	—
Stock-based compensation expense	18,389	26,341
Impairment of acquired in-process research and development	15,696	—
Non-cash income tax benefit	(2,109)	—
Gain from sale of priority review voucher	—	(110,000)
Non-cash interest income	—	(934)
Changes in operating assets and liabilities:		
Inventory	—	(12,674)
Prepaid expenses and other assets	(3,668)	(1,259)
Trade and other receivables	11,682	(17,326)
Accounts payable and accrued expenses	4,842	(8,023)
Deferred rent	2,480	—
Deferred revenue	(2,758)	94,872
Net cash (used in) provided by operating activities	(75,878)	6,855
Cash flows from investing activities:		
Proceeds from sale of priority review voucher	—	110,000
Payment for license agreement	—	(2,000)
Purchase of acquired in-process research and development	(3,457)	—
Purchases of marketable securities	(66,537)	(232,045)
Proceeds from maturities of marketable securities	126,367	220,112
Purchases of property and equipment	(7,221)	(8,129)
Net cash provided by investing activities	49,152	87,938
Cash flows from financing activities:		
Proceeds from exercise of options	5,168	11,746
Purchase of treasury stock	(471)	(2,794)
Proceeds from issuance of common stock under ESPP	—	762
Payments on long-term debt	(150)	(155)
Net cash provided by financing activities	4,547	9,559
Effect of exchange rate changes on cash and cash equivalents	68	(14)
Net (decrease) increase in cash and cash equivalents	(22,111)	104,338
Cash and cash equivalents, beginning of period	58,923	96,748
Cash and cash equivalents, end of period	$36,812	$201,086
Supplemental disclosure of cash flow information:		
Property and equipment purchases included in accounts payable and accrued expenses	$1,422	$4,566
One Drexel Plaza lease cost included in other liabilities	$—	$722

See accompanying notes to the unaudited consolidated financial statements.

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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 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.

In December 2017, the U.S. Food and Drug Administration (FDA) approved LUXTURNA™ (voretigene neparvovec-rzyl) for the treatment of patients with viable retinal cells and confirmed biallelic RPE65 mutation-associated retinal dystrophy.

(2) Development-stage risks

Although the Company had net income in the quarter ended June 30, 2018, the Company has incurred net losses since inception and expects to incur net losses for the foreseeable future. The Company had an accumulated deficit of $477.1 million as of June 30, 2018. The Company anticipates incurring additional losses until such time, if ever, that it can generate significant sales of LUXTURNA and its other product candidates in development. Additional financing may be needed by the Company to fund its operations and to commercially develop its other 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 of the Company's proposed future products; (iii) the success of the commercialization of LUXTURNA; (iv) the timely and successful completion of additional financing; and (v) 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 subsidiaries 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, 2018, its results of operations for the three and six months ended June 30, 2017 and 2018 and cash flows for the six months ended June 30, 2017 and 2018. Operating results for the three and six months ended June 30, 2018 are not necessarily indicative of the results that may be expected for the year ending December 31, 2018 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 consolidated financial statements and related notes as of and for the year ended December 31, 2017 included in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2017.

(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) Trade and other receivables

Trade accounts receivable are recorded at gross value, and reserves for other sales-related allowances, such as discounts, rebates, services and insurance co-pay assistance, are included in accrued expenses on the Company's consolidated balance sheets.

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(d) Inventory

Inventory is stated at the lower of cost or net realizable value and consists of those costs incurred following FDA approval of LUXTURNA. Cost is determined using the first-expired, first-out (FEFO) method. The Company reserves for potentially excess, dated or obsolete inventories based on an analysis of inventory on hand compared to forecasts of future sales. Based on management's assessment, no such inventory reserve is necessary as of June 30, 2018.

Inventory consisted of the following (in thousands):

	June 30, 2018
Raw materials	$1,663
Work in process	10,994
Finished goods	17
	$12,674

(e) Fair value of financial instruments

Management believes that the carrying amounts of the Company’s financial instruments, including cash equivalents, trade and other receivables, accounts payable and accrued expenses, approximate fair value due to the short-term nature of those instruments. Management believes the carrying value of debt approximates fair value as the interest rates are reflective of the rate the Company could obtain on debt with similar terms and conditions.

(f) Net product sales

LUXTURNA is distributed in the United States through two distribution models: (1) the traditional buy-and-bill model where the treatment center purchases and pays for the product and then submits a claim to the payer; and (2) the Company's innovative contracting and distribution model, branded Spark PATH (Pioneering Access to Healthcare), which includes options for direct-to-payer contracting and outcomes-based rebates.

The Company’s net product sales represent total gross product sales in the United States less allowances for estimated prompt-payment discounts, service fees and insurance co-payment assistance. Allowances are established based on contractual terms and management’s reasonable estimates, as well as the expectation that 100% of the prompt-payment discounts will be earned. Product shipping and handling costs and distributor reporting fees are included in cost of product sales. All sales are recognized when control is transferred, which follows the Company’s verification of a scheduled LUXTURNA treatment.

The Company’s product return policy is to provide non-monetary credit or product replacement. As the product is sold in direct relation to a scheduled treatment, Company management estimates that there is minimal risk of product return, including the risk of product expiration.

(g) Contract revenue

Under certain of the Company’s licensing, supply and collaboration agreements, it is entitled to receive payment upon the achievement of contingent milestone events or the performance of obligations. The Company recognizes revenue based on guidance in Accounting Standards Codification (ASC) 606, Revenue from Contracts with Customers.

Prior to 2018, the Company generated revenue solely through license and collaborative arrangements. In the first quarter of 2018, the Company adopted ASC 606. The adoption of this standard resulted in no cumulative adjustment to the Company’s consolidated financial statements.

ASC 606 applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services in an amount that reflects the consideration the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize

revenue when (or as) the entity satisfies a performance obligation. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the

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goods or services promised within each contract and determines those that are performance obligations and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

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.

(h) Net income (loss) per common share

Basic net income (loss) per common share is determined by dividing net income (loss) by the weighted average number of common shares outstanding during the period. For the three and six months ended June 30, 2018, diluted net income per share is determined by dividing net income by the weighted average number of common shares adjusted for the dilutive effect of common stock equivalents. For the three and six months ended June 30, 2017, common stock equivalents have been excluded from the calculation of diluted net loss per share because their effect would be anti-dilutive. Therefore, the weighted average shares outstanding used to calculate both basic and diluted net loss per share are the same for the three and six months ended June 30, 2017.

A reconciliation of basic and diluted net income (loss) per common share is as follows (in thousands, except share and per share data):

	Three months ended June 30,		Six months ended June 30,	
	2017	2018	2017	2018
Numerator:				
Net income (loss)	$(74,360)	$ 80,165	$(126,649)	$ 33,792
Denominator:				
Weighted average shares	30,968,450	37,254,003	30,870,740	37,150,693
Effect of dilutive options and restricted stock	—	1,448,595	—	1,234,404
Weighted average dilutive shares	30,968,450	38,702,598	30,870,740	38,385,097
Basic net income (loss) per common share	$(2.40)	$ 2.15	$(4.10)	$ 0.91
Diluted net income (loss) per common share	$(2.40)	$ 2.07	$(4.10)	$ 0.88

The following potentially dilutive securities have been excluded from the computations of diluted weighted average shares outstanding as of June 30, 2017 and 2018 as they would be anti-dilutive:

	June 30, 2017	June 30, 2018
Unvested restricted common shares	680,653	69,914
Stock options issued and outstanding	4,288,562	395,430

(i) 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, 2018 represents the net excess of rent expense over the actual cash paid for rent plus tenant improvement allowances received.

(j) Other comprehensive loss

The Company follows the provisions of FASB ASC 220, Comprehensive Income, which establishes standards for the reporting and display of comprehensive income and its components. Comprehensive income (loss) is defined to

include all changes in equity during a period except those resulting from investments by owners and distributions to owners. Comprehensive income

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(loss) includes gains and losses related to changes in the fair value of available for sale securities and foreign currency translation.

The accumulated balances related to each component of other comprehensive income (loss) are summarized as follows (in thousands):

	Net unrealized (loss) gain on available for sale securities	Foreign currency translation adjustments	Accumulated other comprehensive loss
Balance as of December 31, 2017	$ (5,964)	$ 50	$ (5,914)
Cumulative adjustment to prior accumulated deficit	5,002	—	5,002
Current period other comprehensive income (loss)	306	(37)	269
Balance as of June 30, 2018	$ (656)	$ 13	$ (643)

(k) Recent accounting pronouncements

In February 2016, the FASB issued Accounting Standards Update (ASU) 2016-02, “Leases.” ASU 2016-02 requires that lease arrangements longer than 12 months result in an entity recognizing an asset and liability. ASU 2016-02 is effective for interim and annual periods beginning after December 15, 2018, and early adoption is permitted. The Company currently is evaluating the impact of the updated guidance on the Company's consolidated financial statements.

In May 2014, the FASB issued a new standard, ASC 606, regarding the accounting for, and disclosures of, revenue recognition, with an effective date for annual and interim periods beginning after December 15, 2017. ASC 606 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 allowable adoption methods are the full retrospective method, which requires the standard to be applied to each prior period presented, or the modified retrospective method which requires the cumulative effect of adoption to be recognized as an adjustment to opening retained earnings in the period of adoption. The Company adopted ASC 606 using the modified retrospective method and the adoption had no cumulative adjustment to its consolidated financial statements as it relates to the Pfizer Inc. (Pfizer) collaboration agreement discussed in note 13. For the six months ended June 30, 2018, the impact of the adoption of ASC 606 resulted in the recognition of $14.0 million and $5.1 million in contract revenue and cost of contract revenue, respectively, that would not have been recognized under prior revenue recognition guidance in effect during 2017.

In January 2016, the FASB issued ASU No. 2016-01, "Financial Instruments-Overall: Recognition and Measurement of Financial Assets and Financial Liabilities". ASU 2016-01 changes accounting for equity investments, financial liabilities under the fair value option, and presentation and disclosure requirements for financial instruments. ASU 2016-01 does not apply to equity investments in consolidated subsidiaries or those accounted for under the equity method of accounting. In addition, the FASB clarified guidance related to the valuation allowance assessment when recognizing deferred tax assets resulting from unrealized losses on available-for-sale debt securities. Equity investments with readily determinable fair values will be measured at fair value with changes in fair value recognized in net income. Companies have the option to either measure equity investments without readily determinable fair values at fair value or at cost, adjusted for changes in observable prices, minus impairment. Changes in measurement under either alternative will be recognized in net income. Companies that elect the fair value option for financial liabilities must recognize changes in fair value related to instrument-specific credit risk in other comprehensive

income. Companies must assess valuation allowances for deferred tax assets related to available-for-sale debt securities in combination with their other deferred tax assets. The Company adopted this guidance effective January 1, 2018, and the adoption required an adjustment of $5.0 million to accumulated deficit, which was related to an equity security investment on the consolidated balance sheet.

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(4) Marketable securities

The following table summarizes the available-for-sale securities held at December 31, 2017 and June 30, 2018 (in thousands):

Description	Amortized cost	Unrealized gains	Unrealized losses	Fair value
December 31, 2017				
U.S. government agency	$222,179	$ —	$ (640)	$221,539
Corporate securities	$227,238	$ —	$ (5,323)	$221,915
June 30, 2018				
U.S. government agency	$229,645	$ 2	$ (392)	$229,255
Corporate securities	$229,086	$ 5	$ (2,653)	$226,438

No available-for-sale securities held as of June 30, 2018 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 (in thousands):

	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, 2017:			
Assets:			
Money market funds (included in cash and cash equivalents)	$90,348	—	—
Corporate securities (included in cash and cash equivalents)	$5,548	—	—
Marketable securities - U.S. government agencies	$221,539	—	—
Marketable securities - corporate securities	$220,020	$ 1,895	—
At June 30, 2018:			
Assets:			
Money market funds (included in cash and cash equivalents)	$200,441	—	—
Marketable securities - U.S. government agencies	$229,255	—	—
Marketable securities - corporate securities	$226,438	—	—

(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, 2018 consisted of money market funds.

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(b) Marketable securities

The Company classifies its marketable security investments as available-for-sale securities and the securities are stated at fair value. There were no material realized gains or losses recognized on the maturity of available-for-sale securities during the six months ended June 30, 2018 and, as a result, the Company did not reclassify any amount out of accumulated other comprehensive loss for the same period. In addition, as part of the license and stock purchase agreements entered into with Selecta Biosciences, Inc. (Selecta) (note 13), the Company purchased restricted common shares of Selecta. The investment is classified as available-for-sale and is stated at fair value, and changes in fair value are recognized in the consolidated statements of operations and comprehensive income (loss).

(6) Sale of priority review voucher

In May 2018, the Company sold the rare pediatric disease priority review voucher (PRV) it received from FDA in connection with the U.S. approval of LUXTURNA to Jazz Pharmaceuticals Ireland Limited for consideration of $110.0 million. The proceeds from the sale of the PRV were recognized as a gain on the sale of an intangible asset, within other income on the consolidated statements of operations and comprehensive income (loss), as the PRV did not have a carrying value on the Company's consolidated balance sheet at the time of sale.

(7) Impairment of acquired in-process research and development

The acquired in-process research and development (IPR&D) asset was an indefinite-lived intangible asset and was assessed for impairment annually, or more frequently if impairment indicators existed. During the three months ended June 30, 2017, the Company determined that it would no longer pursue product candidates utilizing the technology acquired from Genable Technologies, Ltd. in March 2016 and, accordingly, recorded a non-cash impairment charge of $15.7 million within its consolidated statements of operations and comprehensive income (loss). Additionally, the Company recognized an income tax benefit of $1.0 million related to the reversal of the deferred tax liability associated with the IPR&D during the three months ended June 30, 2017.

(8) Accrued expenses

Accrued expenses consist of the following (in thousands):

	December 31, 2017	June 30, 2018
Compensation and benefits	$ 15,012	$9,465
Consulting and professional fees	4,846	9,984
Research and development	2,809	2,352
Other	2,030	2,048
Total accrued expenses	$ 24,697	$23,849

(9) 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.

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 the next 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.

Additionally, in 2014, 200,000 restricted shares of common stock were issued to The Trustees of the University of Pennsylvania (Penn) in connection with a license agreement, of which 175,000 shares have vested. The remaining shares were canceled during the six months ended June 30, 2018.

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For the six months ended June 30, 2017, the Company recorded compensation expense of $20 thousand and $0.8 million in selling, general and administrative expense and research and development expense, respectively, related to the restricted shares. For the six months ended June 30, 2018, the Company recorded an immaterial amount of compensation expense in selling, general and administrative expense and $2.2 million of expense in research and development expense related to the restricted shares.

The following table summarizes restricted stock activity:

	Number of shares
Nonvested shares at December 31, 2017	100,834
Shares canceled	(25,000)
Shares vested	(75,834)
Nonvested shares at June 30, 2018	—

(10) 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 2018, 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 1,485,322 shares. As of June 30, 2018, 1,238,056 shares were available for future grants under the 2015 Plan.

In January 2018, 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 371,330 shares. The 2015 ESPP provides participating employees with the opportunity to purchase an aggregate of 1,137,539 shares of common stock. For the six months ended June 30, 2018, 13,463 shares were issued under the 2015 ESPP.

Stock-based compensation expense

Stock-based compensation expense by award type was as follows (in thousands):

	Six months ended June 30,	
	2017	2018
Stock options	$13,952	$15,558
Restricted stock	3,466	8,262
Employee stock purchase plan	178	359
	$17,596	$24,179

Of the $24.2 million of stock-based compensation expense incurred during the six months ended June 30, 2018, $10.2 million is classified as research and development expense and $14.0 million is classified as selling, general and administrative expense in the consolidated statements of operations and comprehensive income (loss). Of the $17.6 million of stock-based compensation expense incurred during the six months ended June 30, 2017, $7.2 million is classified as research and development expense and $10.4 million is classified as selling, general and administrative expense in the consolidated statements of operations and comprehensive income (loss).

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Stock options

The following table summarizes stock option activity:

	Number of options	Weighted-average exercise price
Outstanding at December 31, 2017	3,522,874	$ 40.11
Granted	671,500	$ 52.02
Exercised	(284,454)	$ 41.29
Canceled	(86,110)	$ 51.02
Outstanding at June 30, 2018	3,823,810	$ 41.87
Vested at June 30, 2018	1,830,098	$ 32.88

Restricted stock

The following table summarizes restricted common stock activity:

	Number of shares	Weighted-average grant date fair value
Nonvested shares at December 31, 2017	697,667	$ 63.40
Shares granted	491,500	$ 54.44
Shares vested	(141,368)	$ 59.08
Shares canceled	(56,184)	$ 61.79
Nonvested shares at June 30, 2018	991,615	$ 59.67

(11) Related-party transactions

As of December 31, 2017, and June 30, 2018, the Children's Hospital of Philadelphia (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 six months ended June 30, 2017, and 2018, the Company recorded $0.3 million and $0.6 million, respectively, of selling, general and administrative expense related to the reimbursement of such patent costs in the accompanying consolidated statements of operations and comprehensive (income) loss.

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. The Company recorded $3.3 million as research and development expense in each of the six months ended June 30, 2017, and 2018.

As of December 31, 2017, $0.3 million and $1.4 million were recorded in accrued expenses and accounts payable, respectively, as amounts due to CHOP. As of June 30, 2018, $0.1 million and $1.0 million were recorded in accrued expenses and accounts payable, respectively, as amounts due to CHOP.

(12) Commitments and contingencies

In November 2016, the Company entered into a lease agreement for approximately 49,000 square feet of office space in Philadelphia, Pennsylvania, that will terminate on March 31, 2027. Under this lease, the Company received $1.6 million of tenant improvement allowances during 2017. In January 2017, the Company amended its lease for office space in Philadelphia to lease an additional 24,800 square feet that commenced on January 1, 2018, and terminate on December 31, 2028. In November 2017, the Company amended this lease to accelerate the termination date of

approximately 50,000 square feet of

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office space, with such termination to occur, at the latest, in December 2022. The Company recorded an expense of $6.9 million associated with the change in termination date in 2017. As of June 30, 2018, $4.4 million is recorded as long-term other liabilities and $1.7 million is recorded as current other liabilities on the accompanying consolidated balance sheet related to the termination expense.

The following table reconciles the termination cost discussed above (in thousands):

	Balance as of December 31, 2017	Recognized during the six months ended June 30, 2018	Balance as of June 30, 2018
Contract termination liability	$6,827	$758	$6,069

In November 2017, the Company entered into a lease for a new research facility at One Drexel Plaza in Philadelphia, Pennsylvania for approximately 108,000 square feet through June 2033.

Based on the terms of the lease agreement for One Drexel Plaza, the Company has construction period risks during the construction period and the Company is deemed the owner of the building (for accounting purposes only) during the construction period. Accordingly, the Company recorded an asset of $35.0 million at December 31, 2017, representing the Company's leased portion of the building, and recorded a corresponding liability. Upon completion of leasehold improvement construction, the Company may not meet the sale-leaseback criteria for de-recognition of the building asset and liability. Therefore, the lease may be accounted for as a financing obligation. The asset will be depreciated over the expected duration of the lease of 15.5 years, and rental payments will be treated as principal and interest payments on the lease financing obligation liability. The underlying accounting for this transaction has no impact on cash flows associated with the underlying lease or construction in process.

At June 30, 2018, the lease financing obligation balance was $34.3 million and was recorded as a long-term other liability on the consolidated balance sheets.

(13) Collaboration and license agreements

(a) Pfizer

In December 2014, the Company entered into a global collaboration agreement with 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 completion date of Phase 1/2 clinical trials). In November 2017, the Company amended its global collaboration agreement with Pfizer. Under the terms of this amendment, the Company has received $15.0 million in payments and is eligible to receive an additional $10.0 million in payments upon completion of certain transition activities. The $25.0 million of consideration is being recognized as revenue over the remaining estimated performance period associated with the global collaboration agreement.

The Company is eligible to receive up to an additional $230.0 million in aggregate milestone payments, $110.0 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.

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In February 2018, the Company entered into a supply agreement with Pfizer to begin production in 2018 for one batch of drug substance expected to be used for Phase 3 development. The Company received $7.0 million upfront and will receive up to $7.0 million upon delivery. The $14.0 million of consideration is being recognized as revenue as batches of the drug substance is completed.

During the six months ended June 30, 2017, and 2018, the Company recognized $2.8 million and $34.1 million of contract revenue, respectively, related to the Company's agreements with Pfizer. During each of the six months ended June 30, 2017 and 2018, the Company recorded $2.1 million as a reduction to research and development expenses for the reimbursement of costs from Pfizer. As of June 30, 2018, there is $1.8 million of current deferred revenue on the consolidated balance sheet related to the Pfizer agreements.

In July 2018, Pfizer announced they have initiated a Phase 3 program following the Company's transfer of responsibility for the hemophilia B gene therapy program to Pfizer.

(b) Novartis

In January 2018, the Company entered into a licensing and commercialization agreement (Novartis License Agreement) with Novartis Pharma AG (Novartis) to develop and commercialize voretigene neparvovec (also known as LUXTURNA) outside the United States. Under the terms of the Novartis License Agreement, the Company has granted Novartis an exclusive right and license, with the right to grant certain sublicenses, under the Company’s intellectual property reasonably necessary or useful for the development or commercialization of LUXTURNA for the treatment, prevention, cure or control of RPE65-mediated inherited retinal disease (IRD) in humans outside the United States. Under the terms of the Novartis License Agreement, the Company received a non-refundable, one-time payment of $105.0 million in the first quarter of 2018, which is included as deferred revenue on the accompanying consolidated balance sheet as of June 30, 2018. The Company is eligible to receive up to an additional $65.0 million in aggregate milestone payments. The Company also is entitled to receive royalty payments at a percentage of net sales on a royalty-region by royalty-region basis, subject to reduction and extension in certain circumstances.

In conjunction with the Novartis License Agreement, the Company and Novartis also entered into a Supply Agreement, under which the Company has agreed to supply all of the commercial supply of voretigene neparvovec required by Novartis, subject to certain conditions. The Supply Agreement continues until the expiration or early termination of the Novartis License Agreement. In addition, either party may terminate the Supply Agreement upon the other party’s uncured material breach of the Supply Agreement, insolvency or bankruptcy. The majority of the $170.0 million of consideration associated with the Novartis License Agreement will be recognized as revenue as the Company sells supply to Novartis.

(c) Selecta

In December 2016, the Company entered into a License and Option Agreement (Selecta License Agreement) with Selecta that provides the Company with exclusive worldwide rights to Selecta’s proprietary Synthetic Vaccine Particles (SVP™) platform technology for co-administration with gene therapy targets. Under the terms of the Selecta License Agreement, Selecta has granted the Company certain exclusive, worldwide, royalty-bearing licenses to Selecta’s intellectual property and know-how relating to its SVP technology to research, develop and commercialize gene therapies for factor VIII, an essential blood clotting protein relevant to the treatment of hemophilia A, which is the initial target under the license. In addition, for a specified period of time, the Company may exercise options to research, develop and commercialize gene therapies utilizing the SVP technology for up to four additional targets, subject to the Company’s payment of the applicable option exercise fee, in a range of $1.4 million to $2.0 million depending on the incidence of the applicable indication, to Selecta in each case.

Pursuant to a letter agreement (Letter Agreement), entered into between the Company and Selecta on June 6, 2017, Selecta agreed to reimburse the Company for all costs and expenses related to research and development for any licensed products for a specified amount of time, up to an agreed upon cap. Additionally, the Company has agreed to reimburse Selecta in respect of full-time equivalents and out-of-pocket costs incurred in performing certain tasks or assistance specifically requested by the Company. Selecta retains the responsibility to manufacture the Company’s preclinical, clinical and commercial requirements for the SVP technology, subject to the terms of the Selecta License

Agreement.

In connection with the execution of the Selecta License Agreement, the Company paid Selecta an upfront payment of $10.0 million in December 2016. Additional payments in the aggregate of $5.0 million were paid in June 2017 and October 2017 pursuant to the terms of the Selecta License Agreement and the Letter Agreement. On a target-by-target basis, the Company will be responsible to pay up to an aggregate of $430.0 million in milestone payments for each target, with up to $65.0 million being based on the Company's achievement of specified development and regulatory milestones and up to $365.0 million for commercial milestones, as well as tiered royalties on global net sales at percentages ranging from mid-single to low-double

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digits. For a period of 3 years, the Company has the right to fund up to 50% of any development or regulatory milestone payable to Selecta by issuing to Selecta shares of the Company's common stock having a fair market value equal to the percentage of such development or regulatory milestone, as applicable. The Selecta License Agreement will continue on a country-by-country and product-by-product basis until the expiration of the Company's royalty payment obligations with respect to such product in such country unless earlier terminated by the parties. The Selecta License Agreement may be terminated by the Company for convenience upon 90 days' notice and the Company will not be required to make any payments. Either party may terminate the Selecta License Agreement on a target-by-target basis for material breach with respect to such target.

In connection with the Selecta License Agreement, the Company entered into a Stock Purchase Agreement (SPA) with Selecta pursuant to which the Company purchased 197,238 unregistered shares of Selecta's common stock for $5.0 million in December 2016. An additional 324,362 unregistered shares of Selecta's common stock were purchased for $5.0 million in June 2017, and 205,254 unregistered shares of Selecta's common stock were purchased for $5.0 million in October 2017. These shares are classified as available-for-sale securities as of June 30, 2018.

In December 2016, the Company accounted for the payments under the Selecta License Agreement and SPA as a basket transaction and allocated the $15.0 million in cash payments to the shares of Selecta's common stock and the Selecta License Agreement in the amounts of $3.5 million and $11.5 million, respectively. The Company calculated the $3.5 million allocated for the Selecta shares acquired based on the closing market price on the date of purchase. The Company allocated the remaining $11.5 million to the Selecta License Agreement, which was expensed as acquired in-process research and development as the Company determined there was no alternative future use.

In June 2017, the Company accounted for the payments under the Selecta License Agreement, Letter Agreement and SPA as a basket transaction and allocated the $7.5 million in cash payments to the shares of Selecta's common stock and the Selecta License Agreement in the amounts of $4.4 million and $3.1 million, respectively. The Company calculated the $4.4 million allocated to the Selecta shares acquired based on the closing market price on the date of purchase. The Company allocated the remaining $3.1 million to the Selecta License Agreement, which was expensed as acquired in-process research and development as the Company determined there was no alternative future use.

In October 2017, the Company accounted for the payments under the Selecta License Agreement, Letter Agreement and SPA as a basket transaction and allocated the $7.5 million in cash payments to the shares of Selecta's common stock and the Selecta License Agreement in the amounts of $4.1 million and $3.4 million, respectively. The Company calculated the $4.1 million allocated to the Selecta shares acquired based on the closing market price on the date of purchase. The Company allocated the remaining $3.4 million to the Selecta License Agreement, which was expensed as acquired in-process research and development as the Company determined there was no alternative future use.

(14) Subsequent Event

On July 3, 2018, the Company entered into a credit agreement with Wells Fargo Bank, National Association (Wells Fargo) as lender (the Credit Agreement), pursuant to which Wells Fargo extended a $50.0 million term loan to the Company, which bears interest at one-month LIBOR plus 0.65%, which rate is converted to a fixed rate per annum of 3.463% under the swap agreement discussed below. The term loan was fully drawn on the date of the Credit Agreement and matures on July 3, 2023. Through June 2019, the Company will only be obligated to make monthly interest payments with respect to the term loan. Thereafter, the term loan will amortize in equal monthly installments through maturity. In connection with the Credit Agreement, the Company entered into a cash collateral and swap agreement with Wells Fargo on July 3, 2018.

In August 2018, the Company entered into a Dedicated Manufacturing and Commercial Supply Agreement (the Brammer Agreement) with Brammer Bio MA, LLC (Brammer), pursuant to which Brammer has agreed to manufacture and supply certain products for the Company for clinical trial and commercialization purposes. During the term of the agreement, the Company will have access to a dedicated, specified portion of the manufacturing capacity in Brammer's manufacturing facility located in Cambridge, Massachusetts, as well as non-dedicated capacity at Brammer's facilities for manufacturing and other supply-related activities. Under the Brammer Agreement, the Company will make an upfront payment of $4.0 million to Brammer.

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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 in conjunction with our consolidated financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q and the audited consolidated financial statements and notes thereto and management's discussion and analysis of financial condition and results of operations for the year ended December 31, 2017, included in our Annual Report on Form 10-K that was filed with the SEC on February 27, 2018. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Quarterly Report on Form 10-Q, our actual results could differ materially from the results described in, or implied by, these forward-looking statements.

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 potentially one-time, life-altering treatments. The goal of gene therapy is to overcome the effects of a malfunctioning, disease-causing gene. Gene therapies 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. We have built a pipeline of gene therapy product candidates that are directed to the retina, the liver and the central nervous system.

In December 2017, the U.S. Food and Drug Administration, or FDA, approved LUXTURNA™ (voretigene neparvovec-rzyl) for the treatment of patients with viable retinal cells and confirmed biallelic RPE65 mutation-associated retinal dystrophy, a genetic blinding condition caused by mutations in the RPE65 gene. LUXTURNA is the first FDA-approved gene therapy for a genetic disease, the first and only pharmacological treatment for an inherited retinal disease, or IRD, and the first adeno-associated virus, or AAV, vector gene therapy approved in the United States. LUXTURNA will be manufactured at our manufacturing facility located in Philadelphia, which is the first licensed manufacturing facility in the United States for a gene therapy treating an inherited disease. LUXTURNA has received orphan product designation and, upon approval, we received a rare pediatric disease priority review voucher, or PRV, that we sold to Jazz Pharmaceuticals Ireland Limited in May 2018. In January 2018, we entered into a licensing and commercialization agreement with Novartis Pharma AG, or Novartis, for the development and commercialization of investigational voretigene neparvovec outside the United States. We continue to advance the regulatory review by the European Medicines Agency, or EMA, and expect a Committee for Medicinal Products for Human Use, or CHMP, opinion in September, with a formal action by European Commission in the fourth quarter of 2018.

We are supporting the appropriate use of LUXTURNA in the United States through small, targeted commercial and medical affairs groups to build and promote access to the product. LUXTURNA will be administered by leading retinal surgeons at selected treatment centers in the United States that specialize in treating IRDs. In January 2018, we announced two novel payer programs to help ensure eligible patients in the United States have access to LUXTURNA: (i) an innovative contracting model, which includes an option for direct-to-payer contracting; and (ii) an outcomes-based rebate arrangement with a short-term efficacy measure and a long-term durability measure.

We have two gene therapy product candidates, to which we retain global commercialization rights, in clinical development: (i) SPK-7001, targeting choroideremia, or CHM, currently in a Phase 1/2 clinical trial, and (ii) SPK-8011, our lead product candidate in the SPK-FVIII program for hemophilia A, currently in Phase 1/2 clinical trial. A third clinical-stage product candidate, SPK-9001, our lead product candidate in the SPK-FIX program for hemophilia B, was recently transitioned to Pfizer, Inc., or Pfizer, per our license agreement. Pfizer recently announced the initiation of a Phase 3 program for SPK-9001, now referred to as PF-06838435 or fidanacogene elaparvovec. SPK-7001 is our lead product candidate for the treatment of CHM, an IRD caused by mutations in the REP-1 gene. We have completed enrollment of ten participants in two dose cohorts of our Phase 1/2 trial for SPK-7001 and continue to follow subjects in the trial. In July 2017, we completed enrollment of five additional subjects in the trial who are at an earlier stage of disease. To date, SPK-7001 has been well tolerated and we have not observed any

product candidate-related serious adverse events, or SAEs, in this trial. We have received orphan product designation for SPK-7001 for the treatment of CHM in both the United States and the European Union.

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. In July 2016, FDA granted breakthrough therapy designation to SPK-9001, the lead product candidate in our SPK-FIX program. In July 2018, we transitioned the program to Pfizer for Phase 3 development.

Throughout 2017 and 2018, Pfizer and we provided periodic updates at medical meetings on the progress of the Phase 1/2 trial of SPK-9001. Most recently, in May 2018 at the World Federation of Hemophilia, or WFH, we presented interim data, as of the May 7, 2018, cutoff date, that the annualized bleeding rate for the fifteen trial subjects had been reduced by 98% and the annualized infusion rate had been reduced by 99%. The data also demonstrated evidence of long-term durability with more

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than two years of follow-up in some participants, with infrequent and transient transaminase elevations. No participants developed factor IX inhibitors and no SAEs or thromboembolic events have been reported. In February 2018, we entered into a supply agreement with Pfizer for production of one batch of SPK-9001 drug substance.

In our SPK-FVIII program for the treatment of hemophilia A, we initiated a dose-escalating Phase 1/2 clinical trial for our lead product candidate, SPK-8011, in 2017. As of a July 13, 2018, data cutoff date, we had enrolled 12 participants in the trial - two at a dose of 5 x 10^{11} vector genomes (vg)/kilogram of body weight, three at a dose of 1 x 10^{12} vg/kg and seven at a dose of 2 x 10^{12} vg/kg. Across all 12 participants at the three doses tested, we saw a 97% reduction in annualized bleeding rate (ABR) and a 97% reduction in annualized infusion rate (AIR). We also saw evidence of stable, durable expression, with no decline in plateau factor VIII activity levels in both participants in the 5 x 10^{11} vg/kg cohort, both of which have been followed for greater than one year. We demonstrated a dose response, with the higher dose leading to higher factor VIII levels across the three dose cohorts.

As of the data cutoff date, five of the participants in the 2 x 10^{12} vg/kg cohort had factor VIII activity levels between 16% and 49%, with follow-up ranging from 12 to 30 weeks. The mean factor VIII activity for these five participants was 30%, based on average factor VIII levels post-12 weeks after infusion. These five participants have reduced their overall ABR by 100% and their AIR by 100% (calculated based on data after week four). The other two participants in this cohort had an immune response that caused their factor VIII activity levels to decline to less than 5%.

Clinically, both participants have progressed from prophylactic to on-demand treatment and have seen meaningful reductions in ABR and AIR. One of these participants did not rapidly respond to oral steroids and elected to be admitted to the hospital to receive two intravenous infusions of methylprednisolone rather than having the infusions on an outpatient basis. The event subsequently resolved, but the admission to the hospital met the criteria for a serious adverse event.

Across the study, seven of the 12 participants received a tapering course of oral steroids in response to an alanine aminotransferase (ALT) elevation above patient baseline, declining factor VIII levels and/or positive IFN-gamma enzyme-linked immunospots (ELISPOTs). For these seven participants, steroids led to a normalization of ALT and ELISPOTs. For all but the two participants mentioned above in the 2 x 10^{12} vg/kg dose cohort, oral steroids led to a stabilization of factor VIII levels. We plan to incorporate a course of prophylactic steroids going forward in the development program.

We have scaled our mammalian cell-based suspension process to a 200 liter single-use bioreactor level and have achieved initial yields that are supportive of our future clinical and commercial requirements. We will confirm the comparability of material manufactured with this suspension process to material manufactured with our adherent process as part of our Phase 1/2 study. We also have secured dedicated manufacturing capacity at Brammer Bio's facility in Cambridge, Massachusetts.

In August, we announced plans to take SPK-8011 at a dose of 2 x 10^{12} vg/kg into Phase 3 clinical trials, beginning with a run-in study in the fourth quarter of 2018. In February 2018, FDA granted SPK-8001 breakthrough therapy designation. We retain global commercialization rights to the SPK-FVIII program.

We have several product candidates in various stages of preclinical development. The RPE65 and CHM genes are two of more than 220 genes that have been identified to cause IRDs. We have several preclinical programs targeting other IRDs. We are developing other liver-directed gene therapies, including SPK-GAA for Pompe disease, an inherited lysosomal storage disorder caused by an enzyme deficiency that leads to accumulation of glycogen in cells, for which there are shortcomings in current enzyme replacement standard of care. We are developing neurodegenerative disease product candidates that are intended to address TPP1 deficiency, which is a form of Batten disease, and Huntington's disease, among others. We have received orphan product designation in the United States for SPK-TPP1 for the treatment of CLN2 disease (neuronal ceroid lipofuscinosis (NCL)) caused by TPP1 deficiency.

With the sale of our PRV in May 2018, we were profitable for the three and six months ended June 30, 2018, although with the exception of such periods, we have incurred net losses since inception. We have an accumulated deficit of $477.1 million as of June 30, 2018. Substantially all of our net losses resulted from costs incurred in connection with our research and development programs and from selling, general and administrative expenses associated with our operations. For the six months ended June 30, 2017 and 2018, we incurred $65.3 million and $55.6 million of research and development expenses, respectively, and $48.1 million and $63.2 million of selling, 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 commercialize any approved products, including LUXTURNA. Because of the numerous risks and uncertainties associated with product development and commercialization, 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.

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Through June 30, 2018, 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 $858.2 million.

- On February 4, 2015, we completed our initial public offering, or IPO, of 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. The aggregate net proceeds received by us were $168.9 million, net of underwriting discounts and commissions and offering expenses.
- On December 28, 2015, we closed a follow-on offering of 2,266,995 shares of common stock at a price to the public of $47.00 per share with net proceeds received by us of $99.4 million, net of underwriting discounts and commissions and offering expenses.
- On June 20, 2016, we closed a follow-on offering of 3,025,000 shares of common stock at a price to the public of $45.00 per share with net proceeds received by us of $127.6 million, net of underwriting discounts and commissions and offering expenses.
- On August 9, 2017, we closed a follow-on offering of 5,296,053 shares of common stock at a price to the public of $76.00 per share with net proceeds received by us of $379.9 million, net of underwriting discounts and commissions and offering expenses.

Financial operations overview

Revenue

Product Sales

LUXTURNA is distributed in the United States through two distribution models: (1) the traditional buy-and-bill model where the treatment center purchases and pays for the product and then submits a claim to the payer; and (2) our innovative contracting and distribution model, branded Spark PATH (Pioneering Access to Healthcare), which includes options for direct-to-payer contracting and outcomes-based rebates.

Our net product sales represent total gross product sales in the United States less allowances for estimated prompt-payment discounts, service fees and insurance co-payment assistance. Allowances are established based on contractual terms and management's reasonable estimates, as well as the expectation that 100% of the prompt-payment discounts will be earned. Product shipping and handling costs and distributor reporting fees are included in cost of product sales. All sales are recognized when control is transferred, which follows our verification of a scheduled LUXTURNA treatment.

Our product return policy is to provide non-monetary credit or product replacement. As the product is sold in direct relation to a scheduled treatment, we estimate that there is minimal risk of product return, including the risk of product expiration.

During the six months ended June 30, 2018, we recognized $6.7 million in net product sales. Gross sales were $7.6 million, net of $0.9 million of product sales allowances. We expect that net product sales of LUXTURNA will fluctuate quarter over quarter, in particular as we continue to build and promote access. Net product sales for the six months ended June 30, 2018, may not be representative of our sales for any future six month period.

Contract Revenues

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, which completion occurred in July 2018. 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. In November 2017, we amended our global collaboration agreement with Pfizer. Under the terms of this amendment, we have received $15.0 million in payments and are eligible to receive an additional $10.0 million. In February 2018, we entered into a supply agreement with Pfizer to begin production in 2018 for one batch of drug substance expected to be used for Phase 3 development. We received $7.0 million upfront and will receive up to $7.0 million upon delivery. In July 2018, Pfizer announced the initiation of a Phase 3 program following our transfer of responsibility for the hemophilia B gene therapy program to Pfizer.

During the six months ended June 30, 2017 and 2018, we recognized $2.8 million and $34.1 million of contract revenue, respectively, related to our Pfizer agreements and, as of June 30, 2018, there was $1.8 million of current deferred revenue included on our consolidated balance sheet.

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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;
- 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:

- expanding our medical affairs group;
- the Phase 1/2 clinical trials for SPK-7001 and SPK-8011;
- research and development for our preclinical programs; 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” in 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 of any product candidate.

Selling, general and administrative expenses

Selling, general and administrative expenses consist primarily of salaries and related costs, including stock-based compensation and travel expenses, for our employees in operational, finance, legal, business development, commercial and human resource functions. Other selling, 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 selling, general and administrative expenses will increase in the future as we increase our headcount to support our continued growth and the commercialization of our approved products. We also anticipate increases in expenses related to audit, legal, regulatory and tax-related services associated with maintaining compliance as a public company, director and officer insurance premiums and investor relations costs. With the approval of our first product, LUXTURNA in December 2017, we have incurred, and anticipate incurring further, increases in payroll and related expenses as a result of our commercial operations, especially as they relate to sales and marketing.

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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 consolidated 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. Since our Annual Report on Form 10-K, which was filed with the SEC on February 27, 2018, we have added or updated the following accounting policies because we determined them to be the most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Revenue recognition

Prior to 2018, we generated revenue solely through license and collaboration arrangements. In the first quarter of 2018, the Company adopted Accounting Standards Codification, or ASC, 606, Revenue from Contracts with Customers. The adoption of this guidance resulted in no cumulative adjustment to the Company's consolidated financial statements.

ASC 606 applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services in an amount that reflects the consideration the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess the goods or services promised within each contract and determine those that are performance obligations and assess whether each promised good or service is distinct. We then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Product sales

LUXTURNA is distributed in the United States through two distribution models: (1) the traditional buy-and-bill model where the treatment center purchases and pays for the product and then submits a claim to the payer; and (2) our innovative contracting and distribution model, branded Spark PATH, which includes options for direct-to-payer contracting and outcomes-based rebates.

Our net product sales represent total gross product sales in the United States less allowances for estimated discounts, service fees and insurance co-payment assistance. Allowances are established based on contractual terms and management's reasonable estimates, as well as the expectation that 100% of the prompt-payment discounts will be earned. Product shipping and handling costs and distributor reporting fees are included in cost of product sales. All sales are recognized when control is transferred, which follows our verification of a scheduled LUXTURNA treatment.

Our product return policy is to provide non-monetary credit or product replacement. As the product is sold in direct relation to a scheduled treatment, we estimate that there is minimal risk of product return, including the risk of product expiration.

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Results of operations

Comparison of the three months ended June 30, 2017 and 2018

	Three months ended June 30,	
	2017	2018
	(in thousands)	
Revenues:		
Product sales, net	$ —	$ 4,314
Contract revenue	1,483	20,871
Total revenues	1,483	25,185
Operating expenses:		
Cost of product sales	—	269
Cost of contract revenue	—	4,242
Research and development	32,989	25,524
Acquired in-process research and development	3,070	—
Impairment of acquired in-process research and development	15,696	—
Selling, general and administrative	26,729	29,749
Total operating expenses	78,484	59,784
Loss from operations	(77,001)	(34,599)
Unrealized gain on equity investments	—	2,255
Interest income, net	532	2,521
Other income	—	110,000
Income (loss) before income taxes	(76,469)	80,177
Income tax benefit (expense)	2,109	(12)
Net income (loss)	$ (74,360)	$ 80,165

Revenues

In the three months ended June 30, 2018, we recognized $25.2 million in total revenues, of which $4.3 million was net sales of LUXTURNA and $20.9 million was associated with our agreements with Pfizer. In the three months ended June 30, 2017, we recognized $1.5 million in total revenues associated with our Pfizer agreement.

Cost of product sales

Cost of product sales in the three months ended June 30, 2018, was $0.3 million, and consists of manufacturing, shipping and other costs, as well as royalties. A substantial portion of the inventory sold during the period was produced prior to FDA approval and, therefore, was expensed previously as research and development.

Cost of contract revenue

Cost of contract revenue in the three months ended June 30, 2018, was $4.2 million, and consists of manufacturing and other costs associated with our contract agreements.

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Research and development expenses

Our research and development expenses for the three months ended June 30, 2018 were $25.5 million compared with $33.0 million for the three months ended June 30, 2017. The $7.5 million decrease was due to a decrease of $6.2 million in internal research and development expenses and $1.3 million in external research and development expenses. The $6.2 million decrease in internal research and development expenses primarily was due to salaries and other costs associated with LUXTURNA, which were allocated to inventory upon FDA approval. The $1.3 million decrease in external research and development expenses was primarily due to a $2.5 million decrease in expenses related to LUXTURNA and a $1.4 million decrease in our SPK-CHM and SPK-FIX clinical programs. These decreases were offset by an increase of $2.6 million in expenses related to our hemophilia A program.

The following table summarizes our research and development expenses by product candidate or program for the three months ended June 30, 2017 and 2018:

	Three months ended June 30,	
	2017	2018
	(in thousands)	
External research and development expenses:		
LUXTURNA	$ 3,149	$ 637
SPK-CHM	519	236
SPK-FIX	1,168	52
SPK-FVIII	970	3,559
Programs in preclinical development	2,415	2,470
Total external research and development expenses	8,221	6,954
Total internal research and development expenses	24,768	18,570
Total research and development expenses	$ 32,989	$ 25,524

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.

Acquired in-process research and development expense

Our acquired in-process research and development expense for the three months ended June 30, 2017 was $3.1 million. This amount represents a payment related to a license agreement and a portion of the payment related to a stock purchase agreement entered into with Selecta Biosciences, Inc., or Selecta, that provides us with exclusive worldwide rights to Selecta's proprietary Synthetic Vaccine Particles (SVP™) platform technology for co-administration with gene therapy targets. We recognized this amount as acquired-in-process research and development because additional research and development efforts and marketing approval are required in order to commercialize the licensed technology.

Impairment of acquired in-process research and development expense

During the three months ended June 30, 2017, we determined that we would no longer pursue product candidates utilizing the technology acquired from Genable Technologies, Ltd., or Genable, in March 2016 and, accordingly, we recorded a non-cash impairment charge of $15.7 million. Additionally, we recognized an income tax benefit of $1.0 million related to the reversal of the deferred tax liability associated with the acquired in-process research and development during the three months ended June 30, 2017. We did not incur an impairment of acquired in-process research and development expense during the three months ended June 30, 2018.

Selling, general and administrative expenses

Selling, general and administrative expenses for the three months ended June 30, 2018 were $29.7 million, compared with $26.7 million for the three months ended June 30, 2017. Selling, general and administrative expenses consisted primarily of salaries and related costs, including stock-based compensation, legal and patent costs, facility costs and other professional fees.

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The $3.0 million increase primarily was due to an increase of $3.4 million in salaries and related costs, including stock-based compensation, due to increased headcount primarily to support the LUXTURNA launch and an increase of $0.3 million in legal and patent expenses, professional fees and other operating costs. These increases were offset by a decrease of $0.7 million in launch activities for LUXTURNA.

Other income

We recognized $110.0 million of other income during the three months ended June 30, 2018, for the sale of our rare pediatric disease PRV.

Comparison of the six months ended June 30, 2017 and 2018

	Six months ended June 30,	
	2017	2018
	(in thousands)	
Revenues:		
Product sales, net	$—	$6,733
Contract revenue	2,758	34,128
Total revenues	2,758	40,861
Operating expenses:		
Cost of product sales	—	390
Cost of contract revenue	—	5,111
Research and development	65,338	55,633
Acquired in-process research and development	3,457	—
Impairment of acquired in-process research and development	15,696	—
Selling, general and administrative	48,142	63,238
Total operating expenses	132,633	124,372
Loss from operations	(129,875)	(83,511)
Unrealized gain on equity investments	—	2,619
Interest income, net	1,117	4,706
Other income	—	110,000
Income (loss) before income taxes	(128,758)	33,814
Income tax benefit (expense)	2,109	(22)
Net income (loss)	$(126,649)	$33,792

Revenues

In the six months ended June 30, 2018, we recognized $40.8 million in total revenues, of which $6.7 million was net sales of LUXTURNA and $34.1 million was associated with our agreements with Pfizer. In the six months ended June 30, 2017, we recognized $2.8 million in total revenues associated with our Pfizer agreement.

Cost of product sales

Cost of product sales in the six months ended June 30, 2018, was $0.4 million, and consists of manufacturing, shipping and other costs, as well as royalties. A substantial portion of the inventory sold during the period was produced prior to FDA approval and, therefore, was expensed previously as research and development.

Cost of contract revenue

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Cost of contract revenue in the six months ended June 30, 2018, was $5.1 million, and consists of manufacturing and other costs associated with our contract agreements.

Research and development expenses

Our research and development expenses for the six months ended June 30, 2018 were $55.6 million compared with $65.3 million for the six months ended June 30, 2017. The $9.7 million decrease was due to a $6.5 million decrease in internal research and development expenses, primarily due to salaries and other costs associated with LUXTURNA, which were allocated to inventory upon FDA approval, and a decrease of $3.2 million in external research and development. The decrease in external research and development primarily was due to a $5.0 million decrease in expenses related to LUXTURNA, a $2.3 million decrease in our SPK-CHM and SPK-FIX clinical programs and a $0.2 million decrease in programs in preclinical development. These decreases were offset by an increase of $4.2 million in expenses related to our hemophilia A program.

The following table summarizes our research and development expenses by product candidate or program for the six months ended June 30, 2017 and 2018:

	Six months ended June 30,	
	2017	2018
	(in thousands)	
External research and development expenses:		
LUXTURNA	$7,128	$2,150
SPK-CHM	1,084	522
SPK-FIX	2,001	285
SPK-FVIII	2,214	6,455
Programs in preclinical development	4,591	4,367
Total external research and development expenses	17,018	13,779
Total internal research and development expenses	48,320	41,854
Total research and development expenses	$65,338	$55,633

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.

Acquired in-process research and development expense

Our acquired in-process research and development expense for the six months ended June 30, 2017 was $3.5 million. This amount represents a payment related to a license agreement and a portion of the payment related to a stock purchase agreement entered into with Selecta that provides us with exclusive worldwide rights to Selecta's proprietary SVP™ platform technology for co-administration with gene therapy targets. We recognized this amount as acquired-in-process research and development because additional research and development efforts and marketing approval are required in order to commercialize the licensed technology.

Impairment of acquired in-process research and development expense

During the six months ended June 30, 2017, it was determined that we would no longer pursue product candidates utilizing the technology acquired from Genable in March 2016 and, accordingly, we recorded a non-cash impairment charge of $15.7 million. Additionally, we recognized an income tax benefit of $1.0 million related to the reversal of the deferred tax liability associated with the acquired in-process research and development during the six months ended June 30, 2017. We did not incur an impairment of acquired in-process research and development expense during the six months ended June 30, 2018.

Selling, general and administrative expenses

Selling, general and administrative expenses for the six months ended June 30, 2018 were $63.2 million compared with $48.1 million for the six months ended June 30, 2017. Selling, general and administrative expenses consist primarily of salaries and related costs, including stock-based compensation, legal and patent costs, facility costs and other professional fees. The

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$15.1 million increase primarily was due to an increase of $10.4 million in salaries and related costs, including stock-based compensation, due to increased headcount primarily to support the LUXTURNA launch, an increase of $0.4 million in launch activities for LUXTURNA and $4.4 million in legal and patent expenses, professional fees and other operating costs.

Other income

We recognized $110.0 million of other income during the six months ended June 30, 2018, for the sale of our rare pediatric disease PRV.

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,	
	2017	2018
	(in thousands)	
Net cash (used in) provided by:		
Operating activities	$(75,878)	$6,855
Investing activities	49,152	87,938
Financing activities	4,547	9,559
Effect of exchange rate changes on cash and cash equivalents	68	(14)
Net (decrease) increase in cash and cash equivalents	$(22,111)	$104,338

Net cash (used in) provided by operating activities

The net cash provided by operating activities was $6.9 million for the six months ended June 30, 2018, and consisted of net income of $33.8 million adjusted for non-cash items, including depreciation and amortization expense of $3.1 million, stock-based compensation expense of $26.3 million, non-cash rent income of $1.1 million, a loss on disposal of equipment of $0.1 million and non-cash interest income of $0.9 million. Net cash provided by operating activities also included a net decrease in operating assets and liabilities of $55.6 million. The significant items in the change in operating assets include an increase in trade and other receivables of $17.3 million, primarily due to Pfizer receivables related to our global collaboration and supply agreements and trade receivables related to LUXTURNA sales, an increase of $1.3 million in prepaid expenses and other assets, and an increase of $12.7 million of inventory as a result of the commercialization of LUXTURNA. The significant items in the change in operating liabilities include a decrease in accounts payable and accrued expenses of $8.0 million mainly due to large accruals at year-end related to bonus and other related salary accruals. The change in operating liabilities also includes an increase in deferred revenue of $94.9 million primarily due to the receipt of $105.0 million from entering into a license and commercialization agreement with Novartis in January 2018.

The net cash used in operating activities was $75.9 million for the six months ended June 30, 2017, and consisted of a net loss of $126.6 million adjusted for non-cash items, including a $15.7 million impairment charge on our acquired in-process research and development associated with our Genable acquisition and noncash income tax benefit for the reversal of the deferred tax liability associated with the impairment of $1.0 million, $1.1 million related to our available for sale securities, as well as a $3.5 million in acquired in-process research and development expense, which was recognized as a result of a second payment and equity investment payment related to our collaboration agreement with Selecta. Net cash used in operating activities also included depreciation expense of $2.2 million, stock-based compensation expense of $18.4 million, non-cash rent expense of $0.5 million and a net decrease in operating assets and liabilities of $12.6 million. The significant items in the change in operating assets include a decrease in other receivables of $11.7 million, primarily driven by a $15.0 million payment received on our Pfizer receivable, and an increase of $3.7 million in prepaid expenses and other assets as a result of large prepayments related to preclinical and clinical expenses. The significant items in the change in operating liabilities include an increase in accounts payable

and accrued expenses of $4.8 million mainly due to an increase in accruals related to bonus and other related salary accruals as a result of increased headcount. The change in operating liabilities also includes an increase in deferred rent of $2.5 million related to tenant improvement allowances, and a decrease in deferred revenue of $2.8 million.

Net cash provided by investing activities

Net cash provided by investing activities for the six months ended June 30, 2018, was $87.9 million which included $110.0 million in proceeds from the sale of our PRV, offset by costs related to the net purchases of marketable securities of $12.0 million, the purchase of property and equipment of $8.1 million and a product milestone payment of $2.0 million associated with the first product sale of LUXTURNA.

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Net cash provided by investing activities for the six months ended June 30, 2017, was $49.1 million, consisting of net proceeds from maturities of marketable securities of $59.8 million, offset by purchases of property and equipment of $7.2 million and $3.5 million in payments related to our license agreement with Selecta.

Net cash provided by financing activities

Net cash provided by financing activities for the six months ended June 30, 2018, was $9.6 million, which consisted of $11.7 million from the exercise of stock options and $0.8 million of proceeds from the issuance of common stock under our employee stock purchase plan, offset by $2.8 million for our repurchase of common stock for tax withholding obligations on restricted stock that vested during the six months ended June 30, 2018 and $0.1 million in payments of long-term debt.

Net cash provided by financing activities for the six months ended June 30, 2017, was $4.5 million, which consisted of $5.2 million in proceeds from the exercise of stock options, offset by $0.5 million in purchases of treasury stock related to net settlements of vested stock and $0.2 million in payments on long-term debt.

Funding requirements

We expect our expenses to increase compared to prior periods in connection with our ongoing activities, particularly as we continue to commercialize LUXTURNA, continue research and development, continue and initiate clinical trials and seek regulatory approvals for our product candidates.

The expected use of our cash and cash equivalents and marketable securities of $656.8 million as of June 30, 2018, 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, the timing and outcome of regulatory filings and actions, commercialization of approved products, 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 marketable securities.

Based on our planned use of our cash and cash equivalents and marketable securities, we estimate that such funds will be sufficient to enable us to continue to commercialize LUXTURNA, complete our Phase 1/2 trials for SPK-7001 and SPK-8011, advance certain of our other pipeline product candidates and fund our operating expenses and capital expenditure requirements into 2021. The foregoing estimate does not contemplate the receipt of any milestone payments under our collaborations with Pfizer and Novartis. 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

As of June 30, 2018, 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, 2017.

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, 2018, we had cash and cash equivalents and marketable securities, including our investment in Selecta, of $656.8 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

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immediately and uniformly by 100 basis points from levels as of June 30, 2018, the net fair market value of our marketable securities would have resulted in a hypothetical decline of approximately $2.7 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, 2018. 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 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, 2018, 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

With our increased commercialization efforts for LUXTURNA during the quarter ended June 30, 2018, we have implemented internal controls around inventory and cost of goods sold. There have been no other changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the quarter ended June 30, 2018 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

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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 the beginning 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
Although we had net income in the quarter ended June 30, 2018, we have generally incurred net losses since inception. We expect to incur losses for the foreseeable future and do not expect to maintain the profitability we experienced in the quarter ended June 30, 2018 for the foreseeable future.
Prior to the quarter ended June 30, 2018, we have incurred net losses since inception. Our net loss was $126.6 million and our net income was $33.8 million for the six months ended June 30, 2017 and 2018, respectively. Our net income in the quarter ended June 30, 2018 was largely attributable to the sale of our PRV. As of June 30, 2018, we had an accumulated deficit of $477.1 million. We have financed our operations primarily through private placements of our preferred stock, our IPO, which closed on February 4, 2015, and follow-on offerings which closed on December 28, 2015, June 20, 2016 and August 9, 2017. We received net proceeds from the IPO and follow-on offerings of $775.8 million, after deducting underwriting discounts and commissions and other offering expenses payable by us. We have devoted substantially all our efforts to research and development, including clinical and preclinical development of our product candidates, as well as to building our team and engaging in activities to prepare for commercial launch of LUXTURNA. 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:
- continue to commercially launch LUXTURNA in the United States;
- seek marketing approvals for any of our product candidates that successfully complete clinical trials;
- continue to grow a marketing and distribution infrastructure to commercialize LUXTURNA in the United States, and any product candidates for which we may submit for and obtain marketing approval anywhere in the world;
- continue our clinical development of our product candidates, including our Phase 1/2 clinical trials for SPK-7001 and SPK-8011;
- conduct IND-enabling studies for our preclinical programs;
- initiate additional preclinical studies and clinical trials for our product candidates;
- seek to identify additional product candidates;
- build out additional laboratory and current good manufacturing practices, or cGMP, manufacturing capacity;
- further develop our gene therapy platform;
- further expand our medical affairs activities;
- maintain, expand and protect our intellectual property portfolio; and
- acquire or in-license product candidates and technologies.

LUXTURNA is our only product that has been approved for sale and, to date, it only has been approved in the United States for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy who have viable retinal cells as determined by their treating physicians. Our ability to generate revenue will depend on the success of commercial sales of LUXTURNA. However, the successful commercialization of LUXTURNA in the United States is subject to many risks. LUXTURNA is our first commercial launch, and there is no guarantee that we will be able to do so successfully. There are numerous examples of unsuccessful launches where products fail to meet

expectations of market potential, including

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those by pharmaceutical companies with more experience and resources than us. We do not anticipate our revenue from sales of LUXTURNA alone will be sufficient for us to become profitable.

To become and remain profitable, we must develop and commercialize additional 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 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 generated limited 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 develop and commercialize products.

While we began generating revenue from the sale of LUXTURNA in the first quarter of 2018, we do not expect to achieve profitability unless and until we complete the development of, and obtain the regulatory approvals necessary to commercialize, additional product candidates. Our ability to generate revenues from product sales and achieve profitability depends heavily on our, or our collaborators', success in:

- executing the commercial launch of LUXTURNA;
- maintaining regulatory and marketing approval for LUXTURNA in the United States;
- obtaining regulatory and marketing approval for LUXTURNA in the EU;
- seeking and obtaining regulatory and marketing approvals for product candidates for which we complete clinical trials;
- completing research and preclinical and clinical development of our product candidates and identifying new gene therapy product candidates;
- launching and commercializing product candidates for which we obtain regulatory and marketing approval by expanding our existing sales force, marketing and distribution infrastructure or, alternatively, collaborating with a commercialization partner;
- qualifying for, and maintaining, adequate coverage and reimbursement by government and third-party payers on a timely basis for LUXTURNA and any product candidates for which we obtain marketing approval;
- maintaining and enhancing a sustainable, scalable, reproducible and transferable manufacturing process;
- 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 of our product candidates and the market demand for LUXTURNA and any product candidates for which we obtain marketing approval;
- identifying patients eligible for treatment with LUXTURNA for RPE65-mediated IRD;
- 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.

We anticipate incurring significant costs associated with commercializing LUXTURNA in the United States and any other products for which we receive marketing approval. Even if we are able to generate revenues from sales of

LUXTURNA and any other approved products, we may not become profitable and may need to obtain additional funding to continue operations.

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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 technology, identifying potential product candidates and undertaking preclinical studies and clinical trials of our most advanced product candidates, undertaking the commercial launch of LUXTURNA and establishing collaborations. Although we have commenced the initial phases of the commercialization of LUXTURNA, we have no history of commercializing pharmaceutical products, are still in the process of launching LUXTURNA and, to date, have not generated substantial revenue from the sale of LUXTURNA. 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. We are in the early stages of the process of transitioning 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.

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 and commercialization efforts or other operations.

We expect our expenses to increase as we continue the research and development of, and seek marketing approval for, our product candidates. In addition, we expect to incur significant expenses related to product sales, medical affairs, diagnostics, marketing, manufacturing and distribution to support LUXTURNA and any other products for which we obtain marketing approval. Accordingly, we may need to obtain substantial additional funding for our continuing operations. If we are unable to raise capital on attractive terms, or at all, we could be forced to delay, reduce or eliminate certain of our research and development programs and/or commercialization efforts.

Our operations have consumed significant amounts of capital since inception. As of June 30, 2018, our cash and cash equivalents and marketable securities were $656.8 million. Our operating expenses were $124.4 million for the six months ended June 30, 2018. We expect to incur significant operating expenses for the foreseeable future. We estimate that our cash and cash equivalents and marketable securities as of June 30, 2018, will enable us to fund our operating expenses and capital expenditure requirements into 2021. 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 anticipate.

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

- our execution of our commercial launch of LUXTURNA in the United States;
- the cost and our ability to maintain the commercial infrastructure and manufacturing capabilities required, including product sales, medical affairs, diagnostics, marketing, manufacturing and distribution, to support LUXTURNA in the United States, and any other products for which we receive marketing approval;
- qualifying for, and maintaining adequate coverage and reimbursement by, government and third-party payers on a timely basis for LUXTURNA and any other products for which we obtain marketing approval;
- the costs of preparing and submitting marketing approvals for any of our product candidates that successfully complete clinical trials;
- the costs and timing of manufacturing sufficient supplies of LUXTURNA to meet customer demand;
- the scope, progress, results and costs of drug discovery, recruitment, laboratory testing, preclinical development and clinical trials for our 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;
- revenue received from commercial sales of LUXTURNA and any other products for which we may obtain marketing approval, including amounts reimbursed by government and third-party payers;
- 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 and/or royalty payments 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 product candidates and technologies.

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Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete. We may never generate the necessary data or results required to obtain marketing approval and achieve product sales for any products other than LUXTURNA. In addition, LUXTURNA or any other products for which we obtain marketing approval may not achieve commercial success. Any product revenues from product candidates, 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.

Risks related to LUXTURNA

The commercial success of LUXTURNA depends on the extent to which patients, physicians and payers accept and adopt LUXTURNA as a treatment for inherited retinal disease, or IRD, caused by biallelic mutations in the RPE65 gene.

The commercial success of LUXTURNA depends on the extent to which patients, physicians and payers accept and adopt LUXTURNA as a treatment for inherited retinal disease, or IRD, caused by biallelic mutations in the RPE65 gene, and we do not know whether our or others' estimates in this regard will be accurate. While we conduct activities to raise awareness around genetic testing and inherited retinal diseases, there is significant uncertainty in the degree of market acceptance of LUXTURNA. In addition, physicians may not prescribe LUXTURNA, and patients may be unwilling to use LUXTURNA, if coverage is not provided or reimbursement is inadequate. Additionally, the use of LUXTURNA in a non-trial setting may result in unexpected, more serious or a greater incidence of adverse reactions that may negatively affect the commercial prospects of LUXTURNA. Furthermore, a significant negative development in any other gene therapy program or our failure to satisfy any post-marketing regulatory commitments and requirements to which we are or may become subject may adversely impact the commercial results and potential of LUXTURNA. We will conduct a post-marketing observational study of patients treated with LUXTURNA to further evaluate the long-term safety of LUXTURNA. If the results of this long-term study negatively change the benefit/risk profile of LUXTURNA, the commercial results of LUXTURNA and potentially any other product for which we receive marketing approval may be substantially diminished.

As part of our plan to market LUXTURNA in the United States through a limited number of centers that specialize in treating IRDs, we have trained vitreoretinal surgeons to perform the surgical procedure necessary to administer LUXTURNA via sub-retinal injection. This procedure requires significant skill and training. In addition, if we are unable to recruit or train, and thereafter retain, sufficient retinal surgeons to perform the procedure properly, the availability of LUXTURNA 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 payers on the benefits of LUXTURNA and 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 LUXTURNA and our other potential products.

We have submitted, and had validated, a marketing authorization application, or MAA, to the EMA for LUXTURNA, but obtaining such approval from the European Commission following the opinion of EMA is a lengthy and expensive process. When a marketing authorization application is submitted to the EMA, a related scientific evaluation is conducted by EMA's CHMP and a scientific opinion is prepared concerning the suitability of the product for authorization. This scientific opinion is sent to the European Commission which, before arriving at a final decision on a marketing authorization application, must consult the Standing Committee on Medicinal Products for Human Use. The Standing Committee is composed of representatives of the EU Members States and chaired by a non-voting European Commission representative. The European Parliament also has a related "droit de regard". The European Parliament's role is to ensure that the European Commission has not exceeded its powers in deciding to grant or refuse

to grant a marketing authorization. In accordance with the centralized procedure, the maximum timeframe for the evaluation of an MAA is 210 days. This excludes clock stops during which additional information or written or oral explanations are provided by the applicant in response to questions posed by the CHMP.

Even if a product candidate is approved, the European Commission 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. We have entered into a licensing and commercialization agreement with Novartis for the development and commercialization of voretigene neparvovec outside of the United States. The commercial success of voretigene neparvovec outside of the United States depends on our ability to obtain approval of the MAA by EMA and Novartis' success at commercializing voretigene neparvovec outside of the United States if and when approved. We have

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limited control over the amount and timing of resources that Novartis will dedicate to the commercialization of voretigene neparvovec, should it receive marketing approval.

If the RPE65-mediated IRD patient population is smaller than we estimate, our product revenues may be adversely affected and our business may suffer.

There are several factors that could contribute to making the actual number of patients who receive voretigene neparvovec 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, likely will diminish the therapeutic benefit conferred by a gene therapy due to irreversible cell death. In addition, our patient identification efforts may not be successful due to operational challenges or erroneous prevalence and incidence assumptions. Lastly, certain patients' immune systems might prohibit the successful delivery of certain gene therapy products to the target tissue, thereby limiting the treatment outcomes.

If we are unable to obtain adequate coverage of LUXTURNA from third-party payers, the adoption of LUXTURNA by physicians and patients may be limited, which could affect our ability to successfully commercialize LUXTURNA.

While we have reached agreement with certain third-party payers regarding our price for LUXTURNA, we still may receive substantial resistance to our pricing from other third-party payers and the public generally. To assist third-party payers and patients in obtaining and covering LUXTURNA, we have proposed novel payment and distribution programs to assist with the cost of LUXTURNA, including direct sales to payers and outcomes-based rebate arrangements. Even with these programs, there may be substantial resistance to the cost of LUXTURNA by third-party payers and the public generally. Additionally, to the extent reimbursement for LUXTURNA is subject to outcomes-based rebate arrangements, we may be liable for rebate payments in the future. Durability is a factor we use for our outcomes-based rebate arrangements and a negative change in our durability data could negatively impact our ability to successfully commercialize LUXTURNA. These novel payment programs may not be sufficient for third-party payers to grant coverage, and if we are unable to obtain adequate coverage of LUXTURNA, the adoption of LUXTURNA by physicians and patients may be limited. This in turn could affect our ability to successfully commercialize LUXTURNA and adversely impact our business, financial condition, results of operations and prospects.

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.

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 products. There can be no assurance that we will not experience problems or delays in developing new products and that such problems or delays will not cause unanticipated costs, or that any such development problems can be solved. Currently, LUXTURNA is the only gene therapy product that has been approved for a genetic disease in the United States and only two such products have been approved in the EU. Although we intend to leverage our experience with LUXTURNA in our preclinical and clinical development of product candidates, we may be unable to reduce development timelines and costs for our other 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 successfully commercializing LUXTURNA and any other products for which we obtain marketing approval on a timely or profitable basis, if at all. 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, the European Commission, EMA, the competent authorities of the EU Member States 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 two gene therapy products for genetic diseases, uniQure N.V.'s Glybera and GlaxoSmithKline plc's Strimvelis, have

received marketing authorization from the European Commission. The marketing authorization for Glybera subsequently expired following the decision of the marketing authorization holder not to apply for a related renewal. LUXTURNA is the only gene therapy product for a genetic disease to have received marketing approval from FDA. We do not yet know if or when it may be authorized by the European Commission. Even if we are successful in developing additional product candidates, it is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for these product candidates in either the United States or the EU, or how long it will take to commercialize any other products for which we receive marketing approval. In addition, the marketing authorization granted by the European Commission may not be indicative of what FDA may require for approval and vice versa.

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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 Tissue and Advanced 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 the National Institute of Health, or NIH, also potentially are subject to review by the Regulatory Affairs Certification, or RAC; however, NIH announced in 2014 that the RAC will 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 approved its initiation. Conversely, FDA can put an 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, the European Commission 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.

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 certain regulatory authorities may not consider the endpoints of our clinical trials to provide clinically meaningful results.

Except for LUXTURNA in the United States, there are no pharmacologic therapies approved to treat IRDs caused by the biallelic RPE65 gene mutations. 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. 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 or preliminary stages of clinical trials.

We have limited safety and limited clinical efficacy data for the use of SPK-7001 and SPK-8011 in humans. There can be no assurance that the results seen in preclinical studies for any of our product candidates ultimately will result in success in 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 changes in regulatory policy or requirements 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 subjects in our clinical trials, which could delay or prevent us from proceeding with clinical trials of our product candidates.

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Identifying and enrolling appropriate subjects to participate in clinical trials of our product candidates is critical to our success. The timing of the beginning and conclusion of clinical trials depends on our ability to recruit subjects to participate and complete clinical development programs. For example, hemophilia trials often take longer to enroll 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. Patients with the disease may be hesitant or unwilling to participate in our gene therapy studies for a variety of reasons: 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. These factors may delay the timeline for recruiting subjects, conducting studies and obtaining regulatory approval of our product candidates. 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.

We may not be able to identify, recruit and enroll a sufficient number of subjects, or those with required or desired characteristics, to complete our clinical trials in a timely manner. 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 subjects;
- 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. For any other product candidate that we successfully develop, we plan to seek initial marketing approvals in the United States and, subsequently, the EU. We may not be able to initiate or continue clinical trials if we cannot enroll a sufficient number of eligible subjects 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 contract research organizations, or CROs, and clinical investigators;
- 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 subjects 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 or 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

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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 agreement or 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 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, after an inspection of our clinical trial operations or trial sites or for any other reason;
- 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 Practice or applicable regulatory guidelines in the EU 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 or to achieve regulatory and commercialization milestones or product 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 or 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 we intended or desired;
- obtain approval with labeling that includes significant product use or distribution restrictions or safety warnings, including contraindications, warnings or precautions;
- 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, or REMS, or a similar risk mitigation strategy;
- be sued for alleged injuries caused to patients taking our products; or
- experience damage to our reputation.

Our product and product candidates and the process for administering our product and 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

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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, which we are unable to mitigate with immuno-suppressive regimens, we may decide or be required to halt or delay further clinical development of our product candidates and our commercial efforts could be materially and adversely affected.

In addition to any potential side effects caused by the product or product candidate, the administration process or related procedures also can cause adverse side effects. If any such adverse events occur, our marketing authorization or 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 LUXTURNA to manage post-operative inflammation related to the standard vitrectomy procedure subjects undergo prior to administration of LUXTURNA. 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.

In addition, FDA could require us to adopt a REMS, and other non-US regulatory authorities could impose other specific obligations as a condition of approval to ensure that the benefits of our product candidates outweigh their risks, which could delay approval or commercial acceptance of our product candidates. A REMS may include, among other things, a communication plan to health care practitioners or patients, and elements to assure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools. Similar risk management programs could be imposed by equivalent authorities in foreign jurisdictions, including by the European Commission.

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 or limitations of use in product labeling;
- 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 by our products to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of LUXTURNA and any other products for which we receive marketing approval and could significantly harm our business, financial condition, results of operations and prospects.

We may be unable to obtain additional orphan drug designations or obtain and maintain orphan drug exclusivity for any product. If our competitors obtain orphan drug exclusivity for products that regulatory authorities determine 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 EU, 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 EU, 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 EU. Additionally, orphan designation is granted for products intended for the

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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 EU would be sufficient to justify the necessary investment in developing the drug or biologic product. Similar "orphan drug" designations exist in some, but not all, jurisdictions outside the EU and the United States.

Upon approval, LUXTURNA was granted orphan drug exclusivity by FDA for the treatment of IRD caused by biallelic mutations to the RPE65 gene. Pursuant to such orphan drug exclusivity in the United States, FDA is precluded, subject to certain exceptions discussed below, from approving another marketing application for a product that constitutes the same drug treating the same indication for a seven-year period, which exclusivity period can be extended by six months under certain circumstances as discussed below. Orphan drug designation does not guarantee orphan drug exclusivity and a designated orphan drug will be denied market approval if it is blocked by the orphan exclusivity of a previously approved orphan product.

LUXTURNA has received an orphan drug designation from the European Commission for the treatment of both LCA and RP due to RPE65 mutations. SPK-9001 has received both breakthrough therapy and orphan drug designation by FDA. SPK-8011 has received breakthrough therapy designation by FDA. SPK-7001 has been granted orphan drug designation by FDA and the European Commission for the treatment of CHM. SPK-TPP1 has been granted orphan product designation by FDA for the treatment 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. 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 disease or condition 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 if it is the same product approved for the same disease or condition for the applicable exclusivity period. The applicable period is seven years in the United States and 10 years in the EU. 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 EU can be reduced to six years if, at the end of the fifth year, it is established that the orphan designation criteria are no longer met, e.g., where 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 maintain orphan drug exclusivity for LUXTURNA or 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 disease or 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 or the exclusivity holder consents to the approval of another product or if the sponsor cannot supply a sufficient quantity of the product. It is unclear what criteria regulatory authorities will use for gene therapies to determine similarity under orphan drug designation. In the EU, 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, if the holder of the marketing authorization for the original orphan medicinal product consents to a

second orphan medicinal product application, or if 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 SPK-9001 for the treatment of hemophilia B and SPK-8011 for the treatment of hemophilia A. 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:

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(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, or the redemption of a Rare Pediatric Disease Priority Review Voucher 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 SPK-9001 and SPK-8011 have been designated as breakthrough therapy product candidates, FDA may later decide that either or both no longer meet the conditions for designation and revoke it or decide that the application for the product will not receive priority review.

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 narrower 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 or conditions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory 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 or they may impose significant limitations in the form of narrow indications, contraindications or a REMS. These regulatory authorities may require warnings or precautions 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 or allow the promotional 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 CE marking, 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, with respect to LUXTURNA, have been permitted by FDA. For future product candidates, however, it may be necessary to use FDA-cleared or FDA-approved diagnostic tests or equivalent tests approved by foreign authorities or CE marked in the EU 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 EU, Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic

medical devices will apply from 2022 and repeal the current applicable provisions. Regulation (EU) 2017/746 will 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.

LUXTURNA, and any of our product candidates for which we obtain regulatory approval, will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, 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 or the specific obligations imposed as a condition for marketing authorization by equivalent authorities in a foreign jurisdiction, particularly by the European Commission, 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-

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marketing testing, including Phase 4 clinical trials, and surveillance to monitor the quality, safety and efficacy of the product. For example, in the United States, 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 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 the Federal Food Drug and Cosmetic Act and implementing regulations and are subject to FDA oversight and post-marketing reporting obligations, in addition to other potentially applicable federal and state laws.

In the EU, the advertising and promotion of our products are subject to EU laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU Member States may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising for medicinal products are consistent with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. The SmPC is the document that provides information to physicians concerning the safe and effective use of the medicinal product. It forms an intrinsic and integral part of the marketing authorization granted for the medicinal product. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion. The off-label promotion of medicinal products is prohibited in the EU. The applicable laws at EU level and in the individual EU Member States also prohibit the direct-to-consumer advertising of prescription-only medicinal products. Violations of the rules governing the promotion of medicinal products in the EU could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on our promotional activities with health care professionals.

In addition, product manufacturers and their facilities may be subject to payment of application and program fees and are subject to continual review and periodic inspections by FDA and other regulatory authorities for compliance with current 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 for LUXTURNA or for any other product following approval, 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;
- 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 demand or require the withdrawal or recall of the product from the market;
- refuse to permit the import or export of products;
- request and publicize a voluntary recall of the product; 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

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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.

Both marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by EMA and the competent authorities of the individual EU Member States both before and after grant of the manufacturing and marketing authorizations. This includes control of compliance with cGMP rules, which govern quality control of the manufacturing process and require documentation policies and procedures. We and our third-party manufacturers would be required to ensure that all of our processes, methods, and equipment are compliant with cGMP. Failure by us or by any of our third-party partners, including suppliers, manufacturers, and distributors to comply with EU laws and the related national laws of individual EU Member States governing the conduct of clinical trials, manufacturing approval, marketing authorization of medicinal products, both before and after grant of marketing authorization, and marketing of such products following grant of authorization may result in administrative, civil, or criminal penalties. These penalties could include delays in or refusal to authorize the conduct of clinical trials or to grant marketing authorization, product withdrawals and recalls, product seizures, suspension, or variation of the marketing authorization, total or partial suspension of production, distribution, manufacturing, or clinical trials, operating restrictions, injunctions, suspension of licenses, fines, and criminal penalties.

In addition, EU legislation related to pharmacovigilance, or the assessment and monitoring of the safety of medicinal products, provides that EMA and the competent authorities of the EU Member States have the authority to require companies to conduct additional post-approval clinical efficacy and safety studies. The legislation also governs the obligations of marketing authorization holders with respect to additional monitoring, adverse event management and reporting. Under the pharmacovigilance legislation and its related regulations and guidelines, we may be required to conduct a burdensome collection of data regarding the risks and benefits of marketed products and may be required to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies, which may be time-consuming and expensive and could impact our profitability. Non-compliance with such obligations can lead to the variation, suspension or withdrawal of marketing authorization or imposition of financial penalties or other enforcement measures.

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 and 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 AAV gene therapies in various indications, including Abeona Therapeutics Inc., Adverum Biotechnologies, Inc., Applied Genetic Technologies Corporation, Asklepios BioPharmaceutical, Inc., Audentes Therapeutics, Inc., BioMarin Pharmaceutical Inc., GenSight Biologics SA, Homology Medicines, Inc., Horama SAS, Lysogene SAS, MeiraGTx Limited, Nightstar Therapeutics plc., PTC Therapeutics, Inc., REGENXBIO, Inc., Sangamo Therapeutics, Inc., Sarepta Therapeutics, Inc., Solid Biosciences, Inc., Ultragenyx Pharmaceuticals, Inc., uniQure N.V. and Voyager Therapeutics, Inc., as well as several companies addressing other methods for delivering or 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 LUXTURNA and any of our product candidates.

For LUXTURNA and our clinical product candidates, the main competitors include:

- LUXTURNA. While no other approved pharmacologic agents exist for patients with RPE65-mediated IRD, 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 patients. Novelion Therapeutics, Inc. (formally 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, including MeiraGTx and Horama SAS. 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 Nightstar Therapeutics plc, or Nightstar, is developing an AAV-based gene therapy for the treatment of choroideremia. Nightstar has obtained orphan product designation in the United States and the European Union for this product candidate for the treatment of choroideremia and has announced that it has initiated a

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Phase 3 trial for choroideremia. We are also aware that 4D Molecular Therapeutics and F. Hoffmann-La Roche AG have pre-clinical programs in process.

- SPK-FIX. The standard of care for moderate to severe hemophilia B patients is an intravenously administered variety of plasma-derived, recombinant or long-acting factor FIX products that are produced by a number of companies, including Pfizer Inc., or Pfizer. Many other companies are developing gene therapies to treat hemophilia B, including Shire PLC, Sangamo Therapeutics, Inc., Freeline Therapeutics and uniQure N.V.

- SPK-FVIII. The standard of care for moderate to severe hemophilia A patients is intravenously administered factor VIII protein or its derivatives that are produced by a number of companies. There are other companies developing gene therapies to treat hemophilia A, including BioMarin Pharmaceutical Inc., Ultragenyx Pharmaceuticals, Inc., in collaboration with Bayer HealthCare, Shire PLC, uniQure N.V., Sangamo Therapeutics, Inc. in collaboration with Pfizer and Telethon Institute for Gene Therapy in collaboration with Sanofi.

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 product or product candidates uneconomical or obsolete, and we may not be successful in marketing our product or 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 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 have submitted, and had validated, an MAA to EMA for LUXTURNA and intend to submit for approval of our product candidates in the EU, 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 EU 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 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 the commercialization of LUXTURNA and our product candidates for which we obtain marketing approval

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If we are unable to expand our market development capabilities or enter into agreements with third parties to market and sell any of our product candidates for which we obtain marketing approval, we may be unable to generate any product revenue.

To successfully commercialize any products that may result from our development programs, we need to continue to expand our market development capabilities, either on our own or with others. The development of our own market development effort is, and will continue to 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 have entered into a license and commercialization agreement with Novartis for the development and commercialization of investigational voretigene neparvovec outside the United States, and we are eligible to receive specified milestone payments and royalties pursuant to that 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.

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 EU and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our products or patients may become increasingly difficult to identify and access, all of which would adversely affect our business, financial condition, results of operations and prospects.

Further, there are several factors that could contribute to making the actual number of patients who receive other 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, 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.

Our business could be affected by government price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product and any of our product candidates that may be approved in the future, which would adversely affect our revenue and results of operations.

We expect that coverage and reimbursement of pharmaceutical drugs may be increasingly restricted both in the United States and internationally. The escalating cost of health care has led to increased pressure on the health care industry to reduce costs. In particular, increased public scrutiny has been placed on wholesale prices of drugs, and such prices continue to be subject to intense political and public debate in the United States and abroad. Government and private third-party payers have proposed health care reforms and cost reductions. A number of federal and state proposals to control the cost of health care, including the cost of drug treatments, have been made in the United States. Specifically, there have been several recent United States Congressional inquiries and proposed federal and state bills

designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drugs. At least seven states have passed legislation related to drug price transparency and many others have pending legislation. In addition, there have been proposals to impose federal rebates on Medicare Part D drugs, which would require federally-mandated rebates on either all drugs dispensed to Medicare Part D beneficiaries or on only those drugs dispensed to certain groups of lower income beneficiaries. In some international markets, the government controls the pricing, which can affect the profitability of drugs. Current government regulations and possible future legislation regarding health care may affect coverage and reimbursement for medical treatment by third-party payers, which may render our product or any product candidates for which we obtain marketing approval not commercially viable or may adversely affect our anticipated future revenues and gross margins.

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We cannot predict the extent to which our business may be affected by these or other potential future legislative or regulatory developments. However, future price controls or other changes in pricing regulation or negative publicity related to the pricing of pharmaceutical drugs generally could restrict the amount that we are able to charge for our future products, which would adversely affect our anticipated revenue and results of operations.

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

The cost of a single administration of gene therapy products can be substantial. We expect that coverage and reimbursement by government and commercial payers will be essential for most patients to be able to afford these treatments. Accordingly, sales of our product, and any product candidates for which we obtain marketing approval, will depend substantially, both domestically and abroad, on the extent to which the prices of such 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 payers. Coverage and reimbursement by a third-party payer may depend upon several factors, including the third-party payer'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 payers is a time-consuming and costly process that could require us to provide to the payer 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.

There is significant uncertainty related to third-party coverage and reimbursement of newly approved products, including potential one-time gene therapies. In the United States, third-party payers, including government payers 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 payers and government payers develop their coverage and reimbursement policies. LUXTURNA has been approved for coverage and reimbursement by the Centers for Medicare and Medicaid Services, or CMS, the agency responsible for administering the Medicare program. We cannot be assured that Medicare or Medicaid will cover any other approved products or provide reimbursement at adequate levels to realize a sufficient return on our investment. Moreover, reimbursement agencies in the EU 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 EU Member States. It is difficult to predict what third-party payers will decide with respect to the coverage and reimbursement for our products for which we obtain marketing approval.

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 EU, 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 and 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.

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Moreover, increasing efforts by government and third-party payers 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 and product candidates. Payers increasingly are considering new metrics as the basis for reimbursement rates, such as average sale price, 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 payers to cover any products for which we obtain marketing approval. We expect to experience pricing pressures in connection with the sale of any products for which we obtain marketing approval 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.

In the EU, each EU Member State may restrict the range of medicinal products for which its national health insurance system provides reimbursement and can control the prices of medicinal products for human use marketed in its territory. As a result, following receipt of marketing authorization in the EU, through any application route, an applicant is required to engage in pricing discussions and negotiations with the competent pricing authority in the individual EU Member States. Some EU Member States operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed upon. Other EU Member States approve a specific price for the medicinal product or may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. The downward pressure on healthcare costs in general, particularly prescription drugs, has become more intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, we may face competition for our product candidates from lower priced products in foreign countries that have placed price controls on pharmaceutical products.

A health technology assessment, or HTA, of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in 24 EU Member States. An HTA is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. An HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost-effectiveness of individual medicinal products as well as their potential implications for the healthcare system. Those elements of medicinal products are compared with other treatment options available on the market. The outcome of an HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product varies between EU Member States. In addition, pursuant to Directive 2011/24/EU on the application of patients' rights in cross-border healthcare, a voluntary network of national authorities or bodies responsible for an HTA in the individual EU Member States was established. The purpose of the network is to facilitate and support the exchange of scientific information concerning HTAs. This may lead to harmonization of the criteria taken into account in the conduct of HTAs between EU Member States and in pricing and reimbursement decisions and may negatively affect price in at least some EU Member States. On January 31, 2018, the European Commission adopted a proposal for a regulation on health technologies assessment. This legislative proposal intends to boost cooperation amongst EU Member States for assessing health technology. If adopted in its current form, the regulation will permit EU Member States to use common HTA tools, methodologies and procedures across the EU, working together in four main areas: joint clinical assessments focusing on the most innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early and continuing voluntary cooperation in other areas.

Ethical, legal and social issues related to genetic testing may reduce demand for LUXTURNA or any other gene therapy products for which we obtain marketing approval.

We anticipate that prior to receiving certain gene therapies, patients would be required to undergo genetic testing. Genetic testing has raised concerns regarding the appropriate utilization and the confidentiality of information provided by genetic testing. Genetic tests for assessing a person's likelihood of developing a chronic disease have focused public attention on the need to protect the privacy of genetic information. For example, concerns have been expressed that insurance carriers and employers may use these tests to discriminate on the basis of genetic information, resulting in barriers to the acceptance of genetic tests by consumers. This could lead to governmental authorities restricting genetic testing or calling for limits on or regulating the use of genetic testing, particularly for diseases for which there is no known cure. Any of these scenarios could decrease demand for LUXTURNA or any other products for which we obtain marketing approval.

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

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Even with the requisite approvals from FDA in the United States, European Commission in the EU and other regulatory authorities internationally, the commercial success of any products for which we obtain marketing approval will depend, in part, on the acceptance of physicians, patients and health care payers of gene therapy products in general, and our product candidates in particular, as medically necessary, effective, safe, and cost-effective. Any product that we commercialize may not gain acceptance by physicians, patients, health care providers/payers 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 of any products for which we obtain marketing approval, will depend on several factors, including:

- the efficacy and safety of such product as demonstrated in clinical trials and subsequently in the market;
- the potential and perceived advantages of such product over alternative treatments;
- the cost of treatment relative to alternative treatments;
- the clinical indications for which such product 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 requirements imposed by FDA, the European Commission 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;
- ethical, social and legal concerns about gene therapy that result in additional regulations restricting or prohibiting our products; and
- sufficient third-party payer coverage and reimbursement.

Even if a potential product displays a favorable benefit/risk profile in clinical trials, market acceptance of the product will not be fully known until after it is launched.

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 and 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 other than LUXTURNA approved for a genetic disease to date in the United States and only two gene therapy products for genetic diseases approved to date in the EU. 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 and product candidates, if approved, prescribing treatments that involve the use of our product and product candidates, if approved, 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 LUXTURNA and any other products for which we obtain marketing approval.

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

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We expect that we will be subject to additional risks in commercializing any of 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 third parties

We have in the past entered, and in the future may enter, into collaborations with third parties to develop or commercialize 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 our licensing and commercialization agreement with Novartis for the development and commercialization of voretigene neparvovec outside of the United States. We 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 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 and as further amended in November 2017, relates to the development and commercialization of product candidates for the treatment of hemophilia B. We entered into a supply agreement with Pfizer in February 2018 to supply Pfizer with one batch of SPK-9001 drug product. In July 2018, we transferred responsibility for our hemophilia B gene therapy program to Pfizer and Pfizer initiated its Phase 3 program.

Our licensing and commercialization agreement with Novartis, into which we entered in January 2018, relates to the development and commercialization of voretigene neparvovec outside of the United States. Under this agreement, we granted Novartis an exclusive right and license for the development and commercialization of voretigene neparvovec in humans outside of the United States. We retain responsibility for seeking and maintaining marketing authorization for LUXTURNA granted by the European Commission, and Novartis is responsible for seeking regulatory approval for voretigene neparvovec outside of the United States and EU. If Novartis fails to devote sufficient financial and other resources to the future development and commercialization of voretigene neparvovec outside the United States, the development and commercialization of voretigene neparvovec outside of the United States could be delayed or could fail, which would result in a delay of receiving milestone payments or royalties with respect to voretigene neparvovec or in our not receiving milestone payments or royalties at all. Novartis has the right to terminate the license agreement at any time upon one year's prior written notice to us. Novartis also may terminate the license agreement in the event there is an uncured material breach of our supply agreement by us, resulting in Novartis taking over manufacturing of voretigene neparvovec, or in the event we undergo a change of control. In addition, if Novartis takes over manufacturing of voretigene neparvovec because of our uncured material breach of the supply agreement, the royalties we receive under the license agreement will be reduced. If Novartis terminates our agreement at any time, because of an uncured material breach of the supply agreement or for any other reason, it would delay or prevent our further development and commercialization of voretigene neparvovec, may materially harm our business and could

accelerate our need for additional capital.

We may enter into additional collaborations with third parties in the future. Our relationships with collaborators, including Pfizer and Novartis, and any future collaborations we enter 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;

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- 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;
- our collaborators may not achieve sales targets and we may not receive significant royalty payments based on sales by our collaborators;
- 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 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. Our collaborators are subject to similar risks with respect to product development, regulatory approval and commercialization and their business, results of operations and financial condition could be harmed should they experience any such risks, which could adversely affect our collaboration.

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

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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 or commercializing certain of our products and 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 products or 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 in our network of internal and external (CDMO) facilities that result in delays in our development or commercialization programs or otherwise adversely affect our business.

We completed construction of our own manufacturing facility in 2014, and we may encounter difficulties in operating this facility. The manufacturing process we use to produce LUXTURNA and our product candidates is complex, novel and has been validated for commercial use only with respect to LUXTURNA in the United States. 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 and 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 or 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, EU 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 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

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attractive development programs. Problems in our manufacturing process or CDMO facilities also could restrict our ability to meet market demand for LUXTURNA, or any product candidates for which we may receive marketing approval, and to meet our supply obligations to Novartis. Under our supply agreement with Novartis, we have agreed to provide all of the commercial supply of LUXTURNA required by Novartis, subject to certain conditions. If we are unable to produce enough product to meet the required demand, or if the product we produce does not satisfy the quality standards set forth in the supply agreement, Novartis may be able to manufacture LUXTURNA, terminate our license agreement and/or pay reduced royalties on LUXTURNA. While we have manufactured sufficient supplies for the commercial launch of LUXTURNA in the United States, we may not be able to manufacture sufficient supplies to continue commercial sales on a long-term basis.

Disruptions in our manufacturing process may delay or disrupt our commercialization efforts.

Our GMP manufacturing facility was approved by FDA for the commercial manufacture of LUXTURNA in December 2017. While our manufacturing facility has been inspected by the appropriate regulatory authorities of the EU Member States, we still need to obtain a manufacturing authorization for the EU. A manufacturing authorization must also be obtained from the appropriate regulatory authorities of the EU Member States in which a facility is established. As an approved facility, we will need to continue 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, contract laboratories or suppliers. 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 may rely on third parties to conduct aspects of our product manufacturing, and these third parties may not perform satisfactorily.

While we produce our commercial supply of LUXTURNA at our own facility, we may rely on third parties for the production of certain materials for our product candidates and, therefore, we can control only certain aspects of their activities. We have manufacturing agreements with third parties that provide for, among other things, production of product candidates for our current and future early stage clinical trials. Under certain circumstances, the other party is entitled to terminate its arrangement with us. If we need to enter into alternative arrangements, it could delay our product development activities. Our reliance on third parties 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 a third party 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 any such third party, 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 enter into 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.

Our 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.

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 or

action of equivalent competent authorities in foreign jurisdictions, 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

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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 us could materially harm our business, financial condition, results of operations and prospects.

If 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 our facility is interrupted, there could be a significant disruption in commercial supply of LUXTURNA or any other product for which we obtain marketing approval, and in clinical supply for our product candidates. This also could affect our ability to meet our supply obligations under our agreement with Novartis. We currently do not have a backup manufacturer for commercial supply of LUXTURNA and have limited back-up manufacturing capacity for clinical trial supply for our product candidates. An alternative manufacturer would need to be qualified, through regulatory filings, which could result in further delay. The regulatory authorities also may require additional clinical 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 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 and adversely affect our ability to meet our supply obligations to Novartis.

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 and other components 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 or product candidates could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could materially and adversely affect our development and commercialization timelines and

our business, financial condition, results of operations and prospects and could adversely affect our ability to meet our supply obligations to Novartis.

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

LUXTURNA and 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

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these intermediate products not complying with stability requirements or specifications. Our product and product candidates must be stored and transported at temperatures within a certain range. If these environmental conditions deviate, our product's and 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, with respect to LUXTURNA or any of our product candidates that may be approved, result in a loss of our market share and negatively affect our business, financial condition, results of operations and prospects.

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 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 and to attract, retain and motivate qualified personnel.

We are 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 for our business, including scientific and technical personnel is, and will continue to 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 or key employees, 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 in connection with the commercialization of LUXTURNA in the United States as well as to manage our operations, continue our research and development activities and, over the longer term, continue to build a commercial infrastructure to support commercialization of any other products for which we obtain marketing approval. Future

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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 and the commercialization of LUXTURNA 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, commercialization and growth goals.

Our employees, principal investigators, consultants, advisors 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, advisors and commercial partners. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the EU 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.

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

Our industry is highly regulated and changes in law may adversely impact our business, operations or financial results. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the PPACA, is a sweeping measure intended to, among other things, expand healthcare coverage within the United States, primarily through the imposition of health insurance mandates on employers and individuals and expansion of the Medicaid program.

Several provisions of the law may affect us and increase certain of our costs. See the risk factor entitled "Failure to comply with reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs could result in additional reimbursement requirements, penalties, sanctions and fines which could have a material adverse effect on our business, financial condition, results of operations and growth prospects" for more information regarding PPACA.

In addition, other legislative changes have been adopted since the PPACA was enacted. These changes include aggregate reductions in Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, following passage of the Bipartisan Budget Act of 2018, will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and, accordingly, our financial operations.

We anticipate that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and an additional downward pressure on the reimbursement our customers may receive for our products. Further, there have been, and there may continue to be, judicial and Congressional

challenges to certain aspects of the PPACA. For example, the U.S. Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Additional legislative and regulatory changes to the PPACA, its implementing regulations and guidance and its policies, remain possible in the 115th U.S. Congress and under the Trump Administration. However, it remains unclear how any new legislation or regulation might affect the prices we may obtain for LUXTURNA or any of our product candidates for which regulatory approval is obtained. Any reduction in reimbursement from Medicare and other government programs may result in a similar

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reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

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.

In the United States, the research, manufacturing, distribution, sale, and promotion of drugs and biologic products are subject to regulation by various federal, state, and local authorities in addition to FDA, including CMS, other divisions of the United States Department of Health and Human Services, or HHS, (e.g., the Office of Inspector General), the United States Department of Justice offices of the United States Attorney, the Federal Trade Commission and state and local governments. Our operations are 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 Anti-Kickback Statute, the federal civil and criminal False Claims Act and Physician Payments Sunshine Act and regulations and equivalent provisions in other countries. These laws apply to, 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 affect our operations include, but are not limited to:

- the federal 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. Liability may be established under the federal Anti-Kickback Statute without proving actual knowledge of the statute or specific intent to violate it. There are a number of statutory exemptions and regulatory safe harbors protecting some common activities from prosecution; however, those exceptions and safe harbors are drawn narrowly. Failure to meet all of the requirements of a particular statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute, but the legality of the arrangement will be evaluated on a case-by-case basis based on the totality of the facts and circumstances. We seek to comply with the exemptions and safe harbors whenever possible, but our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability. Moreover, there are no safe harbors for many common practices, such as educational and research grants or patient assistance programs. Violations of the Anti-Kickback Statute are subject to significant civil, criminal, and administrative penalties, including damages, fines, imprisonment, and exclusion from government-funded healthcare programs like Medicare and Medicaid;
- the federal civil False Claims Act, which prohibits any person from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment of government funds; or knowingly and improperly avoiding, decreasing, or concealing an obligation to pay money to the federal government. In recent years, several pharmaceutical and other healthcare companies have faced enforcement actions under the federal False Claims Act for allegedly submitting false or misleading pricing information to government health care programs and providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have faced enforcement actions for causing false claims to be submitted because of the company marketing a product for unapproved, and thus non-reimbursable, uses. In addition, the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. The civil False Claims Act also permits an individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the statute and to share in any monetary recovery. False Claims Act liability is potentially significant because the statute provides for trebling of proved sustained damages and significant mandatory penalties per false claim. Because of the potential for large monetary exposure, healthcare and pharmaceutical companies often resolve allegations without admissions of liability for significant and material amounts to avoid the uncertainty of treble damages and per claim penalties that may awarded in litigation proceedings. Companies may be required, however, to enter into corporate integrity agreements

with the government, which may impose substantial costs on companies to ensure compliance. Criminal prosecution is possible for making or presenting a false or fictitious or fraudulent claim to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among, other things, executing, or attempting to execute, a scheme to defraud any healthcare benefit program or knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false, fictitious, or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry, in connection with the delivery of, or payment for, healthcare benefits, items, or services;

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- HIPAA and its implementing regulations, which impose 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;
- numerous other federal and state laws and regulations that address privacy and data security, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act, or FTC Act), govern the collection, use, disclosure and protection of health-related and other personal information, many of which differ from each other in significant ways, thus complicating compliance efforts;
- the federal Physician Payment Sunshine Act, being implemented as the Open Payments Program, imposes annual reporting requirements on certain manufacturers of drugs, devices, or biologics for payments and other transfers of value, directly or indirectly, to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. A manufacturer's failure to submit timely, accurately and completely the required information for all payments, transfers of value or ownership or investment interests may result in civil monetary penalties of up to an aggregate of $150,000 per year, and up to an aggregate of $1 million per year for "knowing failures." Manufacturers must submit reports by the 90th day of each calendar year; and
- analogous state laws and regulations, such as state anti-kickback and false claims laws, and state fair trade practices laws may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payers, including private insurers. Several states also require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products in those states and to report gifts and payments to individual health care providers in those states. Some of these states also prohibit certain marketing-related activities, including the provision of gifts, meals, or other items to certain health care providers. Other states have laws requiring pharmaceutical sales representatives to be registered or licensed, and still others impose limits on co-pay assistance that pharmaceutical companies can offer to patients. In addition, several states require pharmaceutical companies to implement compliance programs or marketing codes.

State and federal regulatory and enforcement agencies continue actively to investigate violations of health care laws and regulations, and the United States Congress continues to strengthen the arsenal of enforcement tools. Most recently, the Bipartisan Budget Act of 2018 increased the criminal and civil penalties that can be imposed for violating certain federal health care laws, including the Anti-Kickback Statute. Enforcement agencies also continue to pursue novel theories of liability under these laws. In particular, government agencies have recently increased regulatory scrutiny and enforcement activity with respect to programs supported or sponsored by pharmaceutical companies, including reimbursement and co-pay support, funding of independent charitable foundations and other programs that offer benefits for patients. Several investigations into these programs have resulted in significant civil and criminal settlements.

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. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our financial condition and divert the attention of our management from operating our business.

In the EU, interactions between pharmaceutical companies and physicians are also governed by strict laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct in the individual EU Member States. 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 EU. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of EU Member States, such as the UK Bribery Act 2010. The UK Bribery Act applies to any company incorporated in or "carrying on business" in the UK, irrespective of where in the world the alleged bribery activity occurs, which could have

implications for our interactions with physicians both in and outside of the UK. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain EU Member States must be publicly 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 EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

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EU Member States, Switzerland and other countries have also adopted data protection laws and regulations, which impose significant compliance obligations. In the EU, the collection and use of personal health data is currently governed by the provisions of the General Data Protection Regulation, or the GDPR. The GDPR entered into application on May 25, 2018, repealing the Data Protection Directive and increasing our responsibility and liability in relation to the processing of personal data of EU subjects. The GDPR, together with the national legislation of the individual EU Member States governing the processing of personal data, impose strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. In particular, these obligations and restrictions concern the consent of the individuals to whom the personal data relates, the information provided to the individuals for the consent to be considered valid, the transfer of personal data out of the EU, security breach notifications, the use of third-party processors in connection with the processing of the personal data, confidentiality of the personal data, as well as substantial potential fines for breaches of the data protection obligations. Data protection authorities from the different EU Member States may interpret the GDPR and national laws differently and impose additional requirements, which add to the complexity of processing personal data in the EU.

Guidance on implementation and compliance practices are often updated or otherwise revised. With respect to the transfer of personal data out of the EU, the GDPR provides that the transfer of personal data to countries outside of the European Economic Area that are not considered by the European Commission to provide an adequate level of data protection, including the United States, is permitted only on the basis of specific legal grounds.

The judgment by the Court of Justice of the EU in the Schrems case (Case C-362/14 Maximillian Schrems v. Data Protection Commissioner) determined the safe harbor framework, which was relied upon by many United States entities as a basis for transfer of personal data from the EU to the United States, to be invalid. United States entities therefore, had only the possibility to rely on the alternate procedures for such data transfer provided in the EU Data Protection Directive.

On February 29, 2016, however, the European Commission announced an agreement with the United States Department of Commerce, or the DOC, to replace the invalidated safe harbor framework with a new “Privacy Shield”. On July 12, 2016, the European Commission adopted a decision on the adequacy of the protection provided by the Privacy Shield. The Privacy Shield is intended to address the requirements set out by the Court of Justice of the European Union in its Schrems judgment by imposing more stringent obligations on companies, providing stronger monitoring and enforcement by the DOC and the Federal Trade Commission, and making commitments on the part of public authorities regarding access to information. United States entities have been able to certify to the DOC their compliance with the privacy principles of the Privacy Shield since August 1, 2016 and rely on the Privacy Shield certification to transfer personal data from the EU to the United States.

In October 2016, an action for annulment was brought by three French digital rights advocacy group, La Quadrature du Net, French Data Network and the Fédération FDN (Case T-738/16). The case currently is pending before the Court of Justice of the EU. If the Court of Justice of the EU invalidates the Privacy Shield, it will no longer be possible to rely on the Privacy Shield certification to transfer personal data from the EU to entities in the United States. Adherence to the Privacy Shield is not, however, mandatory. Entities based in the United States are permitted to rely either on their adherence to the Privacy Shield or on the other authorized means and procedures to transfer personal data provided by the GDPR.

To comply with the new data protection rules imposed by the GDPR, we are 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.

If we fail to comply with data protection laws and regulations, we could be subject to government enforcement actions (which could include civil or criminal penalties), private litigation and/or adverse publicity, which could negatively affect our operating results and business.

We may be subject to data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the FTC Act and HIPAA), govern the collection, use, disclosure, and protection of health-related and other

personal information. Failure to comply with data protection laws and regulations could result in government enforcement actions and create liability for us (which could include civil and/or criminal penalties), private litigation and/or adverse publicity that could negatively affect our operating results and business.

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues,

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whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR is a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with any activities falling within the scope of the GDPR.

Failure to comply with reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs could result in additional reimbursement requirements, penalties, sanctions and fines which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We have certain price reporting obligations to the Medicaid Drug Rebate program, Medicare and/or other governmental pricing programs, such as state Medicaid supplemental rebate programs. We participate in the Medicaid Drug Rebate program and are, therefore, required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the states for our drugs under Medicaid and Medicare Part B. Such rebates are based on pricing data reported by us on a monthly and quarterly basis to CMS, the federal agency that administers the Medicaid Drug Rebate program. These data include the AMP and best price, or BP, which, in general, represents the lowest price available from the manufacturer to any entity in the United States in any pricing structure, calculated to include all sales and associated rebates, discounts and other price concessions. Our failure to comply with any required price reporting and rebate payment obligations could negatively impact our financial results and could result in penalties.

The PPACA made significant changes to the Medicaid Drug Rebate program, such as expanding rebate liability from fee-for-service Medicaid utilization to include the utilization of Medicaid managed care organizations as well and changing the definition of AMP. The PPACA also increased the minimum Medicaid rebate, changed the calculation of the rebate for certain innovator products that qualify as line extensions of existing drugs; and capped the total rebate amount at 100% of AMP. Finally, the PPACA requires pharmaceutical manufacturers of branded prescription drugs to pay a branded prescription drug fee to the federal government. Congress could enact additional legislation that further increases Medicaid drug rebates or other costs and charges associated with participating in the Medicaid Drug Rebate program. CMS issued a final regulation, which became effective on April 1, 2016, to implement the changes to the Medicaid Drug Rebate program under the PPACA.

Federal law requires that any company that participates in the Medicaid Drug Rebate program also participate in the Public Health Service’s 340B program in order for federal funds to be available for the manufacturer’s drugs under Medicaid and Medicare Part B. The 340B program requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B “ceiling price” for the manufacturer’s covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The PPACA expanded the list of covered entities to include certain free-standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals, but exempts “orphan drugs” from the ceiling price requirements for these covered entities. The 340B ceiling price is calculated using a statutory formula based on AMP and the rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate program, and, in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. Any additional future changes to the definition of AMP and the Medicaid rebate amount under the PPACA or otherwise could affect our 340B ceiling price calculations and negatively impact our results of operations.

The PPACA obligates the Secretary of the HHS to update the agreement that manufacturers must sign to participate in the 340b program to obligate a manufacturer to offer the 340B price to covered entities if the manufacturer makes the drug available to any other purchaser at any price and to report to the government the ceiling prices for its drugs. The Health Resources and Services Administration, or HRSA, has updated the agreement with participating manufacturers accordingly. The PPACA also obligates the Secretary of the HHS to create regulations and processes to improve the

integrity of the 340B program. On January 5, 2017, HRSA issued a final regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities. The effective date of the regulation has been delayed until July 1, 2019. Implementation of this final rule and the issuance of any other final regulations and guidance could affect our obligations under the 340B program in ways we cannot anticipate. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in an inpatient setting.

Federal law also requires that a company that participates in the Medicaid Drug Rebate program report average sales price information each quarter to CMS for certain categories of drugs that are paid under the Medicare Part B program. Manufacturers calculate the average sales price based on a statutorily defined formula as well as regulations and interpretations of the statute by CMS. CMS uses these submissions to determine payment rates for drugs under Medicare Part B. Statutory or regulatory changes or CMS guidance could affect the average sales price calculations for LUXTURNA or our product

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candidates that achieve regulatory approval and the resulting Medicare payment rate, and could negatively impact our results of operations.

Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by us, governmental or regulatory agencies and the courts. In the case of our AMP and BP reported to the Medicaid Drug Rebate program, if we become aware that our reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the pricing data, we are obligated to resubmit corrected data for up to three years after those data originally were due. Such restatements and recalculations would increase our costs for complying with the laws and regulations governing the Medicaid Drug Rebate program and could result in an overage or underage in our rebate liability for past quarters. Price recalculations also may affect the ceiling price at which we will be required to offer for LUXTURNA or our product candidates that achieve regulatory approval under the 340B program.

We will be liable for errors associated with our submission of pricing data. In addition to retroactive rebates and the potential for 340B program refunds, if we are found to have knowingly submitted any false price information to the government, we may be liable for significant civil monetary penalties per item of false information. If we are found to have made a misrepresentation in the reporting of our average sales price, the Medicare statute provides for significant civil monetary penalties for each misrepresentation for each day in which the misrepresentation was applied. Our failure to submit the required price data on a timely basis could result in a significant civil monetary penalty per day for each day the information is late beyond the due date. Such failure also could be grounds for CMS to terminate our Medicaid drug rebate agreement, pursuant to which we participate in the Medicaid Drug Rebate program. In the event that CMS terminates our Medicaid rebate agreement, federal payments may not be available under Medicaid or Medicare Part B for our covered outpatient drugs.

CMS and the HHS Office of Inspector General have pursued manufacturers that were alleged to have failed to report these data to the government in a timely manner. Governmental agencies may also make changes in program interpretations, requirements or conditions of participation, some of which may have implications for amounts previously estimated or paid. We cannot assure you that our submissions will not be found by CMS or other governmental agencies to be incomplete or incorrect.

In order to be eligible to have its products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by certain federal agencies and grantees, a manufacturer also must participate in the Department of Veterans Affairs Federal Supply Schedule, or FSS, pricing program, established by Section 603 of the Veterans Health Care Act of 1992, or the VHCA. Under this program, the manufacturer is obligated to make its innovator and single source products available for procurement on an FSS contract and charge a price to four federal agencies, Department of Veterans Affairs, or VA, Department of Defense, or DoD, Public Health Service, and Coast Guard, that is no higher than the statutory Federal Ceiling Price, or FCP. The FCP is based on the non federal average manufacturer price, or Non FAMP, which we calculate and report to the VA on a quarterly and annual basis. Pursuant to applicable law, knowing provision of false information in connection with a Non-FAMP filing can subject a manufacturer to significant civil penalties for each item of false information. These obligations also contain extensive disclosure and certification requirements.

Moreover, pursuant to regulations issued by the DoD to implement Section 703 of the National Defense Authorization Act for Fiscal Year 2008, manufacturers are required to provide rebates on utilization of their innovator and single source products that are dispensed to TRICARE beneficiaries by TRICARE network retail pharmacies. The formula for determining the rebate is established in the regulations and is based on the difference between the annual Non-FAMP and the FCP (these price points are required to be calculated by us under the VHCA). The requirements under the FSS and TRICARE programs could reduce the revenue we may generate from any products that are commercialized in the future and could adversely affect our business and operating results.

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of LUXTURNA and any other products 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 as we commercialize LUXTURNA or any other products that we may develop. If we cannot successfully defend ourselves against claims that our product or product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for LUXTURNA and any other products 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 or reduced enrollment of clinical trial participants;

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- the inability to successfully commercialize LUXTURNA and any other products 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/or commercialize an additional product. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

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 and product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. 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 payers 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.

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 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 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. Our manufacturing facility and substantially all of our current supply of product and 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. The size and complexity of our information technology systems, and those of our collaborators, contractors and consultants, and the large amounts of confidential information stored on those systems, make such systems vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third-party

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vendors and/or business partners, or from cyber-attacks by malicious third parties. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cyber-attacks also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient.

While we have not experienced a system failure, accident, cyber-attack or security breach that has resulted in a material interruption in our operations to date, if such an event were to occur, 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. Additionally, any such event that leads to unauthorized access, use or disclosure of personal information, including personal information regarding our patients or employees, could harm our reputation, cause us not to comply with federal and/or state breach notification laws and foreign law equivalents and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information. Security breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. While we have implemented security measures to protect our information technology systems and infrastructure, there can be no assurance that such measures will prevent service interruptions or security breaches that could adversely affect our business and the further development and commercialization of our product and product candidates could be delayed.

Risks related to our intellectual property

Our rights to develop and commercialize LUXTURNA and 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 and 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, financial condition, results of operations and prospects.

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, The Trustees of the University of Pennsylvania, Genethon, the NIH and the University of Iowa Research Foundation, 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.

Furthermore, the research resulting in certain of our licensed patent rights and technology was funded by the United States 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 United States 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 and product candidates and manufacturing technology. Our licensors have

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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 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 and 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. 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, 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.

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 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.

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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.

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.

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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 United States patent rights lack corresponding foreign patents or patent applications. For example, we license a United States 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.

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 or 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 our product or one of our product candidates, the defendant could counterclaim that the patent covering our product or 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 or 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 or 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

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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 LUXTURNA and 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 and 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 LUXTURNA, SPK-CHM, 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 LUXTURNA and our product candidates in our SPK-CHM, SPK-FVIII, SPK-GAA 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 United States patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such United States patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such United States 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 and 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 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 and 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.

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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 United States 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 United States 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 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 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

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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 United States 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 patent protection afforded could be less than we request. We have filed an application seeking patent term extension on our LUXTURNA patent but there is a risk that the patent office will not approve the application. 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 registered trademarks with the USPTO for the mark "SPARK" and the Spark logo and pending trademark applications in the United States and various foreign jurisdictions for marks related to our business. 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 business, financial condition, results of operations

and prospects.

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 LUXTURNA or 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;

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- 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

The sale of a significant number of our total outstanding shares into the market 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. 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 1, 2018, we had outstanding options to purchase an aggregate of 3,759,909 shares of our common stock, of which options to purchase 1,888,270 shares 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 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:

- the commercial success of LUXTURNA;
- results of clinical trials of our product candidates or those of our competitors;

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- 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 and the commercialization of LUXTURNA;
- 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;
- negative publicity around gene therapy in general, LUXTURNA or our product candidates;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors; and
- general economic, industry and market conditions.

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.

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 and commercialization of our product and 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.

We incur substantial 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, and particularly since December 31, 2016, when we ceased being an Emerging Growth Company, we incur 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 are required to furnish a report by our management on our internal control over financial reporting, including 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

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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 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.

We received aggregate net proceeds from the offering of $168.9 million, after deducting underwriting discounts and commissions and other estimated offering expenses payable by us. None of the underwriting discounts and commissions or other offering expenses were incurred or paid to directors or officers of ours or their associates or to persons owning 10% or more of our common stock or to any affiliates of ours.

As of June 30, 2018, we have used approximately $167.6 million of the net proceeds from the offering primarily to fund research and development, for working capital and for other general corporate purposes. We have not used any of the net proceeds from the offering to make payments, directly or indirectly, to any directors or officers of ours or their associates or to persons owning 10% or more of our common stock or to any affiliates of ours, other than payments in the ordinary course of business to officers for salaries and to non-employee directors as compensation for board or board committee service. 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, 2018, the remaining amount of the net proceeds is included in cash and cash equivalents and marketable securities on the consolidated balance sheet.

Item 5. Other Information

On August 3, 2018, or the Effective Date, we entered into a Dedicated Manufacturing and Commercial Supply Agreement, or the Brammer Agreement, with Brammer Bio MA, LLC, or Brammer, under which Brammer has agreed to manufacture and supply for us certain products to be determined by the parties for clinical trial and commercialization purposes. The parties also may agree that Brammer will provide additional services pursuant to work orders to be mutually agreed to by the parties. During the term of the agreement, we will have access to a specified portion of the manufacturing capacity in Brammer's manufacturing facility located in Cambridge, Massachusetts, that is dedicated to us for Brammer's manufacturing and supply of products to us, or the Dedicated Capacity, as well as non-dedicated capacity at Brammer's facilities for manufacturing and other supply-related activities.
The Brammer Agreement requires that we purchase from Brammer products in amounts that meet or exceed the minimum purchase commitments set forth therein, or to otherwise pay Brammer for all batches of products that would have been manufactured had we placed orders sufficient to satisfy the applicable minimum purchase commitments. We retain the right to source the products from any other supplier.

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We will pay Brammer for each batch of product supplied pursuant to the terms of the Brammer Agreement, and we also will pay Brammer for specified pass-through costs. In addition, we have agreed to pay an annual fee for the Dedicated Capacity, which fee will be paid in equal quarterly increments, with the first such payment due and payable on April 1, 2019 (each such payment, a Capacity Access Payment). We will make an upfront payment of $4.0 million for the Dedicated Capacity, which payment will be credited against future Capacity Access Payments.

The term of the Brammer Agreement commenced on the Effective Date and continues until March 31, 2026, and automatically renews for successive three-year terms unless we notify Brammer of our intention not to renew no less than 24 months prior to the end of the applicable initial term or renewal term. We may terminate the Brammer Agreement prior to the end of the initial term or renewal term upon specified notice and specified payments that reflect our minimum purchase commitment obligations, Capacity Access Payments, and non-cancellable costs during the period prior to the end of the initial term or renewal term. Brammer may terminate the Brammer Agreement for our material breach of the agreement that is not cured within the applicable notice period, in which event we would be obligated to i) make Capacity Access Payments for 24 months if written notice of termination occurs prior to December 31, 2020, or for 12 months if termination occurs on or after December 31, 2020, in either case following written notice of termination, ii) fulfill our purchase obligations under certain order forecasts and in any case no less than our minimum purchase commitment through the remaining term, and iii) pay for certain non-cancellable payments made or otherwise due by or from Brammer. Each party has a termination right in the event of a bankruptcy or liquidation event of the other party.

The foregoing description of the Brammer Agreement does not purport to be complete and is subject to, and qualified by reference to, the Brammer Agreement. We intend to file a copy of the Brammer Agreement with our Quarterly Report on Form 10-Q for the quarter ending September 30, 2018.

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Item 6. Exhibits

The exhibits filed as part of this Quarterly Report on Form 10-Q are set forth on the Exhibit Index below.

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
10.1	Asset Purchase Agreement, dated April 30, 2018 between the Registrant and Jazz Pharmaceuticals Ireland Limited					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, 2018, formatted in XBRL (eXtensible Business Reporting Language): (i) Consolidated Balance Sheets as of December 31, 2017 and June 30, 2018, (ii) Consolidated Statements of Operations and Comprehensive Income (Loss) for the three and six months ended June 30, 2017 and 2018, (iii) Consolidated Statements of Cash Flows for the six months ended June 30, 2017 and 2018 and (iv) Notes to Unaudited Consolidated Financial Statements.					X

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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 8, 2018

SPARK THERAPEUTICS, INC.

By: /s/ Stephen W. Webster
Stephen W. Webster
Chief Financial Officer
(Principal Financial Officer)