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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-Q

(Mark One)

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended September 30, 2016

OR

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

For the transition period from to

Commission file number: 001-35969

PTC Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**04-3416587**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification Number)
100 Corporate Court South Plainfield, NJ	**07080**
(Address of principal executive offices)	(Zip Code)

(908) 222-7000
(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 ☒ 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 (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

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

Large accelerated filer ☒	Accelerated filer ☐
Non-accelerated filer ☐ (Do not check if a smaller reporting company)	Smaller reporting company ☐

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

As of November 1, 2016 there were 34,318,169 shares of Common Stock, $0.001 par value per share, outstanding.

PART I—FINANCIAL INFORMATION

PART II—OTHER INFORMATION

FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form10-Q contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Quarterly Report on Form10-Q, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward looking statements. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “might,” “plan,” “predict,” “project,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue,” and similar expressions are intended to identify forward looking statements, although not all forward looking statements contain these identifying words.

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

- our ability to resolve the matters set forth in the Refuse to File letter we received from the United States Food and Drug Administration, or FDA, in connection with our New Drug Application, or NDA, for Translarna™ (ataluren) for the treatment of nonsense mutation Duchenne muscular dystrophy, or nmDMD, including whether continuation of our appeal under the formal dispute resolution process with the FDA results in successful reversal of the Refuse to File decision in a timely manner, or ever, and in the event that the Refuse to File decision is reversed, whether such reversal results in a timely or successful review of our NDA, and whether we will be required to perform additional clinical and non-clinical trials or analyses at significant cost and whether such trials, if successful, may enable FDA review of an NDA submission by us and, ultimately, may support approval of Translarna for nmDMD in the U.S.;

- the timing and outcome of the opinion of the European Medicines Agency’s, or EMA’s, Committee for Medicinal Products for Human Use, or CHMP, with respect to our request for renewal of our marketing authorization of Translarna for the treatment of nmDMD in the European Economic Area, or EEA, which is subject to annual review and renewal by the European Commission following reassessment of the risk-benefit balance of the authorization by the European Medicines Agency, among other things;

- the nature of any conditions or restrictions or additional obligations, in addition to a potential new clinical trial in nmDMD, that may be placed on any renewal of the marketing authorization by the European Commission in the event that the CHMP issues a positive opinion with respect to renewal;

- our ability to design an acceptable new clinical trial in nmDMD with input from the EMA, including with respect to matters of scope, length, and conduct and, if successfully designed, our ability to enroll, fund, and complete such trial;

- our ability to commercialize Translarna in general and, specifically, as a treatment for nmDMD, including the timing of such commercialization and our ability to successfully negotiate adequate pricing and reimbursement processes on a timely basis, or at all, in the countries in which we have or may obtain regulatory approval;

- our ability to obtain additional and maintain existing reimbursed named patient and cohort early access programs for Translarna for the treatment of nmDMD on adequate terms, or at all;

- our estimates regarding the potential market opportunity for Translarna, including, in general, the size of eligible patient populations and our ability to identify such patients;

- our regulatory submissions, including with respect to timing and outcome of regulatory review and determinations in connection with our submission with the EMA related to a variation to our marketing authorization to include Translarna as a treatment for nonsense mutation cystic fibrosis, or nmCF, as well as our other submissions with regulatory bodies outside of the EEA;

- our estimates regarding expenses, future revenues, third party discounts and rebates, capital requirements and needs for additional financing, including our ability to maintain the level of our expenses consistent with our internal budgets and forecasts and to secure additional funds on favorable terms or at all;

- the timing and conduct of our ongoing, planned and potential future clinical trials and studies of Translarna for the treatment of nmCF, nmDMD, mucopolysaccharidosis type I, or MPS I, aniridia, and Dravet syndrome/CDKL5, each caused by nonsense mutations, as well as our studies in spinal muscular atrophy and our cancer stem cell

program, including statements regarding the timing of initiation, enrollment and completion of the trials and the period during which the results of the trials will become available;

- the rate and degree of market acceptance and clinical utility of Translarna;
- the ability and willingness of patients and healthcare professionals to access Translarna through alternative means if pricing and reimbursement negotiations in the applicable territory do not have a positive outcome, including whether patients in Germany will continue to be able to access Translarna via a reimbursed importation pathway provided under German law and whether such pathway, if utilized, will minimize any access issues for German patients while maintaining a sustainable price;
- the timing of and our ability to obtain additional marketing authorizations for Translarna and our other product candidates, and the ability of Translarna and our other product candidates to meet existing or future regulatory standards;
- our ability to maintain the current label under the marketing authorization in the EEA or expand the approved product label of Translarna for the treatment of nmDMD, whether pursuant to our recently initiated Phase 2 study of Translarna for nmDMD in pediatric patients, or otherwise;
- the timing and scope of our commercial infrastructure expansion, including the growth of our international presence in Europe and in other territories;
- the potential receipt of revenues from future sales of Translarna and other product candidates, including our ability to earn a profit from sales or licenses of Translarna for the treatment of nmDMD and the impact a potential new clinical trial in nmDMD may have on our revenue growth;
- our sales, marketing and distribution capabilities and strategy, including the ability of our third-party manufacturers to manufacture and deliver Translarna in clinically and commercially sufficient quantities and the ability of distributors to process orders in a timely manner and satisfy their other obligations to us;
- our ability to establish and maintain arrangements for the manufacture of Translarna and our other product candidates that are sufficient to meet clinical trial and commercial launch requirements;
- our plans to pursue development of Translarna for additional indications other than nmDMD, nmCF, MPS I, aniridia, and Dravet/CDKL5, caused by nonsense mutations;
- our ability to advance our earlier stage programs, including our cancer stem cell program;
- our plans to pursue research and development of other product candidates;
- the potential advantages of Translarna;
- our intellectual property position;
- the impact of government laws and regulations;
- our competitive position; and
- our expectations with respect to the development and regulatory status of our product candidates and program directed against spinal muscular atrophy in collaboration with F. Hoffmann La Roche Ltd and Hoffmann La Roche Inc., which we refer to collectively as Roche, and the Spinal Muscular Atrophy Foundation, or the SMA Foundation, and our estimates regarding future revenues from achievement of milestones in that program.

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 Part II, Item 1A. Risk Factors that we believe 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 and our Annual Report on Form 10-K for the year ended December 31, 2015 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.

In this Quarterly Report on Form 10-Q, unless otherwise stated or the context otherwise requires, references to “PTC,” “PTC Therapeutics,” “the Company,” “we,” “us,” “our,” and similar references refer to PTC Therapeutics, Inc. and, where appropriate, its subsidiaries. The trademarks, trade names and service marks appearing in this Quarterly Report on Form 10-Q are the property of their respective owners.

All website addresses given in this Quarterly Report on Form 10-Q are for information only and are not intended to be an active link or to incorporate any website information into this document.

PART I—FINANCIAL INFORMATION

Item 1. Financial Statements.

PTC Therapeutics, Inc.
Consolidated Balance Sheets (unaudited)
In thousands (except per share data)

	September 30, 2016	December 31, 2015
Assets		
Current assets:		
Cash and cash equivalents	$ 50,286	$ 58,022
Marketable securities	198,052	280,903
Prepaid expenses and other current assets	4,860	5,930
Trade receivables, net	27,409	11,094
Total current assets	280,607	355,949
Fixed assets, net	7,059	8,974
Deposits and other assets	511	358
Total assets	$ 288,177	$ 365,281
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable and accrued expenses	$ 47,759	$ 45,247
Deferred revenue	910	139
Other current liabilities	257	—
Total current liabilities	48,926	45,386
Long-term debt	96,559	91,848
Other long-term liabilities	2,515	2,046
Total liabilities	148,000	139,280
Stockholders' equity:		
Common stock, $0.001 par value. Authorized 125,000,000 shares; issued and outstanding 34,165,519 shares at September 30, 2016. Authorized 125,000,000 shares; issued and outstanding 33,916,559 shares at December 31, 2015	34	34
Additional paid-in capital	847,700	820,165
Accumulated other comprehensive income (loss)	756	(1,200)
Accumulated deficit	(708,313)	(592,998)
Total stockholders' equity	140,177	226,001
Total liabilities and stockholders' equity	$ 288,177	$ 365,281

See accompanying unaudited notes.

PTC Therapeutics, Inc.
Consolidated Statements of Operations (unaudited)
In thousands (except per share data)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2016	2015	2016	2015
Revenues:				
Net product revenue	$ 22,013	$ 9,772	$ 56,328	$ 21,002
Collaboration and grant revenue	973	4	1,186	3,030
Total revenues	22,986	9,776	57,514	24,032
Operating expenses:				
Research and development	31,396	30,640	91,622	86,768
Selling, general and administrative	23,654	21,368	72,958	56,193
Total operating expenses	55,050	52,008	164,580	142,961
Loss from operations	(32,064)	(42,232)	(107,066)	(118,929)
Interest (expense) income, net	(2,133)	(852)	(6,149)	170
Other expense, net	(786)	(51)	(1,893)	(507)
Loss before income tax expense	(34,983)	(43,135)	(115,108)	(119,266)
Income tax expense	(184)	(88)	(206)	(233)
Net loss attributable to common stockholders	$ (35,167)	$ (43,223)	$ (115,314)	$ (119,499)
Weighted-average shares outstanding:				
Basic and diluted (in shares)	34,088,741	33,908,853	34,002,952	33,528,833
Net loss per share—basic and diluted (in dollars per share)	$ (1.03)	$ (1.27)	$ (3.39)	$ (3.56)

See accompanying unaudited notes.

PTC Therapeutics, Inc.
Consolidated Statements of Comprehensive Loss (unaudited)
In thousands

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2016	2015	2016	2015
Net loss	$ (35,167)	$ (43,223)	$ (115,314)	$ (119,499)
Other comprehensive loss:				
Unrealized (loss) gain on marketable securities, net of tax	(189)	(483)	429	(582)
Foreign currency translation gain (loss)	60	(149)	1,527	192
Comprehensive loss	$ (35,296)	$ (43,855)	$ (113,358)	$ (119,889)

See accompanying unaudited notes.

PTC Therapeutics, Inc.
Consolidated Statements of Cash Flows (unaudited)
In thousands

	Nine Months Ended September 30,	
	2016	**2015**
Cash flows from operating activities		
Net loss	$ (115,314)	$ (119,499)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	2,477	2,079
Change in valuation of warrant liability	44	(152)
Non-cash interest expense	4,487	736
Amortization of premiums on investments	1,610	1,319
Amortization of debt issuance costs	224	37
Share-based compensation expense	26,610	26,130
Benefit for deferred income taxes	(222)	—
Unrealized foreign currency transaction losses, net	1,401	—
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	1,095	(748)
Trade receivables, net	(16,035)	(3,582)
Deposits and other assets	(154)	183
Accounts payable and accrued expenses	2,080	2,871
Other long-term liabilities	682	(69)
Deferred revenue	768	(3,310)
Net cash used in operating activities	(90,247)	(94,005)
Cash flows from investing activities		
Purchases of fixed assets	(540)	(1,764)
Purchases of marketable securities	(73,692)	(134,299)
Sale and redemption of marketable securities	155,582	167,082
Net cash provided by investing activities	81,350	31,019
Cash flows from financing activities		
Proceeds from exercise of options	926	8,689
Debt issuance costs related to convertible notes	—	(4,650)
Proceeds from issuance of convertible notes	—	150,000
Net cash provided by financing activities	926	154,039
Effect of exchange rate changes on cash	235	(89)
Net (decrease) increase in cash and cash equivalents	(7,736)	90,964
Cash and cash equivalents, beginning of period	58,022	49,748
Cash and cash equivalents, end of period	$ 50,286	$ 140,712
Supplemental disclosure of cash information		
Cash paid for interest	$ 4,513	$ —
Cash paid for income taxes	$ 633	$ —
Supplemental disclosures of non-cash information related to investing and financing activities		
Change in unrealized gain (loss) on marketable securities, net of tax	$ 429	$ (582)

See accompanying unaudited notes.

PTC Therapeutics, Inc.
Notes to Consolidated Financial Statements (unaudited)
September 30, 2016
In thousands (except per share data unless otherwise noted)

1. The Company

PTC Therapeutics, Inc. (the “Company” or “PTC”) was incorporated as a Delaware corporation on March 31, 1998. PTC is a global biopharmaceutical company focused on the discovery, development and commercialization of orally administered, small molecule therapeutics targeting an area of RNA biology referred to as post transcriptional control. Post-transcriptional control processes are the regulatory events that occur in cells during and after a messenger RNA molecule is copied from DNA through the transcription process. PTC has discovered all of its compounds currently under development using its proprietary technologies. PTC plans to continue to develop these compounds both on its own and through selective collaboration arrangements with leading pharmaceutical and biotechnology companies. PTC’s internally discovered pipeline addresses multiple therapeutic areas, including rare disorders and oncology.

PTC’s lead product candidate is ataluren, an investigational new drug in the United States, for the treatment of patients with genetic disorders that arise from a type of genetic mutation known as a nonsense mutation. The Company holds worldwide commercialization rights to ataluren for all indications in all territories. The brand name of ataluren is Translarna™.

The Company received conditional marketing authorization from the European Commission in August 2014 for Translarna for the treatment of nonsense mutation Duchenne muscular dystrophy, or nmDMD, in ambulatory patients aged five years and older in the 31 member states of the European Economic Area, or EEA. The marketing authorization is subject to annual review and renewal by the European Commission following reassessment by the European Medicines Agency, or EMA, of the risk-benefit balance of the authorization, or the annual EMA reassessment, as well as the Company’s satisfaction of any conditions and obligations that have been or may be placed upon the marketing authorization. The Company expects that the EMA's Committee for Medicinal Products for Human Use, or CHMP, will adopt an opinion as to whether to renew the Company's marketing authorization by the end of 2016. During 2016, the Company’s revenues have been, and are expected to be, primarily generated from sales of Translarna for the treatment of nmDMD in countries in the EEA where pricing and reimbursement approval is obtained at acceptable levels and in other territories where the Company is permitted to distribute Translarna under reimbursed early access programs, or EAPs. If the Company's marketing authorization in the EEA is not renewed, or the product label applicable to the marketing authorization is materially restricted, the Company would lose all, or a significant portion of, its ability to generate revenue from product sales, whether pursuant to a commercial or an EAP program and throughout all territories. The Company is subject to a number of risks similar to those of other early stage companies, including dependence on key individuals, the difficulties inherent in the development of commercially usable products, the potential need to obtain additional capital necessary to fund the development of its products, and competition from other companies. As of September 30, 2016, the Company had an accumulated deficit of approximately $708.3 million. The Company has financed its operations to date primarily through the private offering in August 2015 of 3.00% convertible senior notes due 2022 (see Note 9), public offerings of common stock in February 2014 and October 2014, its initial public offering of common stock in June 2013, private placements of its convertible preferred stock, collaborations, bank debt, convertible debt financings, grant funding and clinical trial support from governmental and philanthropic organizations and patient advocacy groups in the disease area addressed by the Company’s product candidates.

2. Summary of significant accounting policies

The Company’s complete listing of significant accounting policies are described in Note 2 of the notes to the Company’s audited financial statements as of December 31, 2015 included in the Company’s Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) on February 29, 2016 (2015 Form 10-K).

Basis of Presentation

The accompanying financial information as of September 30, 2016 and for the three and nine months ended September 30, 2016 and 2015 has been prepared by the Company, without audit, pursuant to the rules and regulations of the SEC. Certain information and footnote disclosures normally included in financial statements prepared in accordance with generally accepted accounting principles in the United States (GAAP) have been condensed or omitted pursuant to such rules and regulations. These interim financial statements should be read in conjunction with the Company’s audited financial statements as of December 31, 2015 and notes thereto included in the 2015 Form 10-K.

In the opinion of management, the unaudited financial information as of September 30, 2016 and for the three and nine months ended September 30, 2016 and 2015 reflects all adjustments, which are normal recurring adjustments, necessary to present a fair statement of financial position, results of operations and cash flows. The results of operations for the three and nine month periods ended September 30, 2016 are not necessarily indicative of the results to be expected for the year ended December 31, 2016 or for any other interim period or for any other future year.

Use of estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Significant estimates in these consolidated financial statements have been made in connection with the calculation of net product sales, certain accruals related to the Company's research and development expenses, stock-based compensation, valuation procedures for the convertible notes, allowance for doubtful accounts and the provision for or benefit from income taxes. Actual results could differ from those estimates. Changes in estimates are reflected in reported results in the period in which they become known.

Inventories and cost of product revenue

In 2014, the Company was notified that the European Commission, or EC, granted marketing authorization for Translarna for the treatment of nmDMD in ambulatory patients aged five years and older. The conditional marketing authorization allows the Company to market Translarna for the treatment of nmDMD in the 31 member states of European Economic Area. The launch in these countries is on a country by country basis. This marketing authorization is subject to annual review and renewal by the EC following reassessment by the European Medicines Agency, or EMA, of the risk benefit balance of the authorization, which the Company refers to as the annual EMA reassessment. The authorization was further conditioned on the Company's submission of the final report, including additional efficacy and safety data, from ACT DMD and the Company's ability to implement measures, including pharmacovigilance plans that are detailed in the risk management plan for Translarna that was submitted to EMA. In January 2016, the Company submitted the final ACT DMD report to the EMA. The Company made this submission as a type II variation request that sought to have this initial condition to its marketing authorization removed and a full marketing authorization granted. In February 2016, the Company also submitted a marketing authorization renewal request with the EMA. The annual EMA reassessment process related to the Company's 2016 marketing authorization request is still ongoing and, as of the time of this filing, renewal has not been granted. The Company expects that the EMA's CHMP will adopt an opinion as to whether to renew the Company's marketing authorization for Translarna for the treatment of nmDMD by the end of 2016. Pursuant to applicable regulations, the Company expects that its current marketing authorization status (which was last renewed by the European Commission in the third quarter of 2015) will remain valid while the 2016 annual EMA reassessment is ongoing and until it is concluded with an opinion from the European Commission with respect to renewal of the marketing authorization.

In the event that the Company's marketing authorization renewal request is granted, the Company plans to seek to renew the marketing authorization on an annual basis until any further obligations or conditions that may be placed by the EC on the marketing authorization have been fulfilled and the approval is converted from a conditional approval into a full approval. If the Company fails to satisfy such further obligations or conditions, or if it is determined that the balance of risks and benefits of using Translarna changes materially, the EC could, at the EMA's recommendation, vary, suspend, withdraw or refuse to renew the marketing authorization for Translarna or require additional clinical trials.

There continues to be substantial risk that regulators could suspend or not renew the Company's marketing authorization in the future. As such, as of the date of this filing, the Company has not capitalized inventory given the near-term uncertainty with respect to the long-term utilization of Translarna finished product for commercial use. Had the Company capitalized as inventory all of the its Translarna product that is available for commercial sale on hand as of September 30, 2016, the value of that inventory would have been approximately $1.3 million. In addition, had the Company expensed the cost of Translarna product sold as a cost of sales, the gross profit margin would have been greater than 90%, which the Company believes is consistent with the cost of producing small molecule therapeutics for orphan drug diseases in the pharmaceutical industry. The Company will continue to assess the appropriateness of inventory capitalization based on the outcome of applicable regulatory determinations, including the pending CHMP opinion regarding the potential annual renewal of our marketing authorization in the EEA, which is expected to be issued in 2016 and followed by ratification by the EC in early 2017. In the event the CHMP issues a positive opinion regarding renewal of the marketing authorization, and the EC ratifies such determination, the Company would expect to capitalize inventory and commence the expensing of cost of goods sold.

Revenue Recognition

The Company recognizes revenue when amounts are realized or realizable and earned. Revenue is considered realizable and earned when the following criteria are met: (1) persuasive evidence of an arrangement exists; (2) delivery has occurred or services have been rendered; (3) the price is fixed or determinable; and (4) collection of the amounts due are reasonably assured.

Net Product Sales

The Company's net product sales have consisted solely of sales of Translarna for the treatment of nmDMD in territories outside of the U.S. The Company began recognizing revenue for payments received under the reimbursed EAPs for Translarna in nmDMD patients in select countries in the third quarter of 2014. The Company has now established a pattern of collectability and, since January 2015, the Company recognizes revenue from product sales when there is persuasive evidence that an arrangement exists, title to product and associated risk of loss has passed to the customer, the price is fixed or determinable, collectability is reasonably assured and the Company has no further performance obligations in accordance with Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") Subtopic 605-15, Revenue Recognition—Products.

The Company has recorded revenue on sales where Translarna is available either on a commercial basis or through a reimbursed EAP program. Orders for Translarna are generally received from hospital and retail pharmacies and, in some cases, one of the Company's third-party partner distributors. The Company's third-party partner distributors act as intermediaries between the Company and end users and do not typically stock significant quantities of Translarna. The ultimate payor for Translarna is typically a government authority or institution or a third-party health insurer.

The Company records revenue net of estimated third-party discounts and rebates. Allowances are recorded as a reduction of revenue at the time revenues from product sales are recognized. These allowances are adjusted to reflect known changes in factors and may impact such allowances in the quarter those changes are known.

Collaboration and Grant Revenue

The terms of these agreements typically include payments to the Company of one or more of the following: nonrefundable, upfront license fees; milestone payments; research funding and royalties on future product sales. In addition, the Company generates service revenue through agreements that generally provide for fees for research and development services and may include additional payments upon achievement of specified events.

The Company evaluates all contingent consideration earned, such as a milestone payment, using the criteria as provided by FASB ASC 605-28, Revenue Recognition—Milestone Method. At the inception of a collaboration arrangement, the Company evaluates if a milestone payment is substantive. The criteria requires that (1) the Company determines if the milestone is commensurate with either its performance to achieve the milestone or the enhancement of value resulting from our activities to achieve the milestone; (2) the milestone be related to past performance; and (3) the milestone be reasonable relative to all deliverable and payment terms of the collaboration arrangement. If these criteria are met then the contingent milestones can be considered a substantive milestone and will be recognized as revenue in the period that the milestone is achieved. The Company recognizes royalties as earned in accordance with the terms of various research and collaboration agreements. If not substantive, the contingent consideration is allocated to the existing units of accounting based on relative selling price and recognized following the same basis previously established for the associated unit of accounting.

The Company recognizes revenue for reimbursements of research and development costs under collaboration agreements as the services are performed. The Company records these reimbursements as revenue and not as a reduction of research and development expenses as the Company has the risks and rewards as the principal in the research and development activities.

Allowance for doubtful accounts

The Company maintains an allowance for estimated losses resulting from the inability of its customers to make required payments. The Company estimates uncollectible amounts based upon current customer receivable balances, the age of customer receivable balances, the customer's financial condition and current economic trends. The allowance for doubtful accounts was $0.4 million as of September 30, 2016 and $0 as of December 31, 2015.

Recently issued accounting standards

In May 2014, the FASB issued Accounting Standards Update (ASU) No. 2014-9, "Revenue from Contracts with Customers (Topic 606)". ASU No. 2014-9 will eliminate transaction- and industry-specific revenue recognition guidance under current

GAAP and replace it with a principle-based approach for determining revenue recognition. ASU No. 2014-9 includes the required steps to achieve the core principle that an entity should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The ASU will also require additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. With the issuance of ASU No. 2015-14 in August 2015, the FASB deferred the effective date of the revenue recognition guidance to reporting periods beginning after December 15, 2017. Early adoption of the standard is permitted but not before the original effective date, which was for reporting periods beginning after December 15, 2016. With the issuance of ASU No. 2016-8 in March 2016 and ASU No. 2016-10 in April 2016, the FASB further amended guidance on recording revenue on a gross versus a net basis and on identifying performance obligations and licensing, respectively. The Company expects to adopt this guidance when effective and continues to evaluate the effect that the updated standard, as well as additional amendments, may have on its consolidated financial statements and accompanying notes.

In August 2014, the FASB issued ASU 2014-15, “Presentation of Financial Statements—Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity’s Ability to Continue as a Going Concern”, which defines management’s responsibility to assess an entity’s ability to continue as a going concern, and to provide related footnote disclosures if there is substantial doubt about its ability to continue as a going concern. The pronouncement is effective for annual reporting periods ending after December 15, 2016 with early adoption permitted. The adoption of this guidance is not expected to have a significant impact on the Company’s financial statements.

In April 2015, the FASB issued ASU No. 2015-3, “Interest—Imputation of Interest (Subtopic 835-30): Simplifying the Presentation of Debt Issuance Costs topic of the Codification”. This standard provides a simplified presentation of debt issuance costs and requires that debt issuance costs related to a recognized debt liability to be presented on the balance sheet as a direct deduction from the carrying amount of that debt liability, consistent with debt discounts. The standard is effective for public companies for annual periods beginning after December 15, 2015. The Company adopted the guidance on January 1, 2016 on a retrospective basis and reclassed $2.8 million from “Deposits and other assets” to “Long-term debt” on the balance sheet as of December 31, 2015. The Company’s unamortized debt issuance cost at September 30, 2016 was $2.5 million which is included within “Long-term debt” on the consolidated balance sheet.

In November 2015, the FASB issued ASU No. 2015-17, “Income Taxes (Topic 740): Balance Sheet Classification of Deferred Taxes”. This standard requires all deferred tax assets and liabilities to be classified as non-current on the balance sheet instead of separating deferred taxes into current and non-current amounts. In addition, valuation allowance allocations between current and non-current deferred tax assets are no longer required because those allowances also will be classified as non-current. This standard is effective for public companies for annual periods beginning after December 15, 2016. Earlier application is permitted as of the beginning of an interim or annual reporting period. The Company’s deferred tax assets is provided with full valuation allowance as of September 30, 2016. As such, the Company does not expect that this standard will have a significant impact upon adoption.

In January 2016, the FASB issued ASU No. 2016-1, “Financial Instruments - Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities”. This standard enhances the reporting model for financial instruments, which includes amendments to address aspects of recognition, measurement, presentation and disclosure. The new guidance affects all reporting organizations (whether public or private) that hold financial assets or owe financial liabilities. ASU 2016-1 is effective for years beginning after December 15, 2017, including interim periods within those fiscal years. The Company expects to adopt this guidance when effective and is currently assessing what effect the adoption of ASU No. 2016-1 will have on its consolidated financial statements and accompanying notes.

In February 2016, the FASB issued ASU No. 2016-2, “Leases (Topic 842)”. This standard will require organizations that lease assets with lease terms of more than 12 months to recognize assets and liabilities for the rights and obligations created by those leases on their balance sheets. The ASU will also require new qualitative and quantitative disclosures to help investors and other financial statement users better understand the amount, timing, and uncertainty of cash flows arising from leases. The standard is effective for public companies for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2018, with early adoption permitted. The Company expects to adopt this guidance when effective and is currently assessing what effect the adoption of ASU No. 2016-2 will have on its consolidated financial statements and accompanying notes.

In March 2016, the FASB issued ASU No. 2016-9, “Compensation—Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting”. This standard requires the recognition of all income tax effects of awards in the income statement when the awards vest or are settled, with Additional Paid in Capital (APIC) pools to be eliminated. In

addition, the standard will increase the amount an employer can withhold to cover income taxes on awards and still qualify for the exception to liability classification for shares used to satisfy the employer's statutory income tax withholding obligation as well as allowing companies to elect whether to account for forfeitures of share-based payments by recognizing forfeitures of awards as they occur or estimating the number of awards expected to be forfeited and adjusting the estimate when it is likely to change, as is currently required. This standard is effective for public companies for fiscal years beginning after December 15, 2016 and interim periods within those years, with early adoption permitted but only if all of the guidance is adopted in the same period. The Company expects to adopt this guidance when effective and is currently assessing what effect the adoption of ASU No. 2016-9 will have on its consolidated financial statements and accompanying notes.

In June 2016, the FASB issued ASU No. 2016-13, "Financial Instruments — Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments". This standard requires financial assets measured at amortized cost basis to be presented at the net amount expected to be collected. This standard is effective for public companies who are SEC filers for fiscal years beginning after December 15, 2019, including interim periods within those years. The Company expects to adopt this guidance when effective and is assessing what effect the adoption of ASU 2016-13 will have on its consolidated financial statements and accompanying notes.

In August 2016, the FASB issued ASU No. 2016-15, "Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments". This standard clarifies the presentation of certain specific cash flow issues in the Statement of cash flows. The standard is effective for public companies for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2017, with early adoption permitted. The adoption of this guidance is not expected to have a significant impact on the Company's consolidated financial statements.

3. Fair value of financial instruments and marketable securities

The Company follows the fair value measurement rules, which provides guidance on the use of fair value in accounting and disclosure for assets and liabilities when such accounting and disclosure is called for by other accounting literature. These rules establish a fair value hierarchy for inputs to be used to measure fair value of financial assets and liabilities. This hierarchy prioritizes the inputs to valuation techniques used to measure fair value into three levels: Level 1 (highest priority), Level 2, and Level 3 (lowest priority).

- Level 1—Unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the balance sheet date.

- Level 2—Inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly. Level 2 inputs include quoted prices for similar assets and liabilities in active markets, quoted prices for identical or similar assets or liabilities in markets that are not active, inputs other than quoted prices that are observable for the asset or liability (i.e., interest rates, yield curves, etc.), and inputs that are derived principally from or corroborated by observable market data by correlation or other means (market corroborated inputs).

- Level 3—Inputs are unobservable and reflect the Company's assumptions as to what market participants would use in pricing the asset or liability. The Company develops these inputs based on the best information available.

Cash equivalents and investments are reflected in the accompanying financial statements at fair value. The carrying amount of grant and collaboration receivables, accounts payable and accrued expenses, and debt approximates fair value due to the short-term nature of those instruments.

Fair value of certain marketable securities is based upon market prices using quoted prices in active markets for identical assets quoted on the last day of the period. In establishing the estimated fair value of the remaining investments, the Company used the fair value as determined by its investment advisors using observable inputs other than quoted prices.

The Company reviews its investments on a periodic basis for other-than-temporary impairments. This review is subjective, as it requires management to evaluate whether an event or change in circumstances has occurred in that period that may have a significant adverse effect on the fair value of the investment.

The following represents the fair value using the hierarchy described above for the Company's financial assets and liabilities that are required to be measured at fair value on a recurring basis as of September 30, 2016 and December 31, 2015:

	September 30, 2016			
	Total	Quoted prices in active markets for identical assets (level 1)	Significant other observable inputs (level 2)	Significant unobservable inputs (level 3)
Marketable securities	$ 198,052	$ —	$ 198,052	$ —
Warrant liability	$ 4	$ —	$ —	$ 4
Stock appreciation rights liability	$ 838	$ —	$ —	$ 838

	December 31, 2015			
	Total	Quoted prices in active markets for identical assets (level 1)	Significant other observable inputs (level 2)	Significant unobservable inputs (level 3)
Marketable securities	$ 280,903	$ —	$ 280,903	$ —
Warrant Liability	$ 48	$ —	$ —	$ 48
Stock appreciation rights liability	$ —	$ —	$ —	$ —

No transfers of assets between Level 1 and Level 2 of the fair value measurement hierarchy occurred during the periods ended September 30, 2016 and December 31, 2015.

The following is a summary of marketable securities accounted for as available-for-sale securities at September 30, 2016 and December 31, 2015:

	September 30, 2016			
	Amortized Cost	Gross Unrealized		Fair Value
		Gains	Losses	
Commercial paper	$ 17,935	$ 53	$ —	$ 17,988
Corporate debt securities	166,119	110	(109)	166,120
Government obligations	13,936	8	—	13,944
	$ 197,990	$ 171	$ (109)	$ 198,052

	December 31, 2015			
	Amortized Cost	Gross Unrealized		Fair Value
		Gains	Losses	
Commercial paper	$ 26,877	$ 80	$ —	$ 26,957
Corporate debt securities	226,959	—	(640)	226,319
Government obligations	27,656	3	(32)	27,627
	$ 281,492	$ 83	$ (672)	$ 280,903

At September 30, 2016 and December 31, 2015, the Company held securities with an unrealized loss position that were not considered to be other-than-temporarily impaired as the Company has the ability to hold such investments until recovery of their fair value. Unrealized gains and losses are reported as a component of accumulated other comprehensive (loss) income in stockholders' equity. As of September 30, 2016 and December 31, 2015, the Company did not have any realized gains/losses from the sale of marketable securities.

Marketable securities on the balance sheet at September 30, 2016 and December 31, 2015 mature as follows:

	September 30, 2016	
	Less Than 12 Months	More Than 12 Months
Commercial paper	$ 17,988	$ —
Corporate debt securities	132,009	34,111
Government obligations	13,944	—
Total Marketable securities	$ 163,941	$ 34,111

	December 31, 2015	
	Less Than 12 Months	More Than 12 Months
Commercial paper	$ 26,957	$ —
Corporate debt securities	140,831	85,488
Government obligations	18,994	8,633
Total Marketable securities	$ 186,782	$ 94,121

The Company classifies all of its securities as current as they are all available for sale and are available for current operations.

Level 3 valuation

The warrant liability is classified in Other long-term liabilities on the Company's consolidated balance sheets. The warrant liability is marked-to-market each reporting period with the change in fair value recorded as a gain or loss within Other expense, net, on the Company's consolidated statements of operations until the warrants are exercised, expire or other facts and circumstances lead the warrant liability to be reclassified as an equity instrument. The fair value of the warrant liability is determined at each reporting period by utilizing the Black-Scholes option pricing model.

The stock appreciation rights (SARs) liability is classified in Other long-term liabilities on the Company's consolidated balance sheets. The SARs liability is marked-to-market each reporting period with the change in fair value recorded as compensation expense on the Company's consolidated statements of operations until the SARS vest. The fair value of the SARs liability is determined at each reporting period by utilizing the Black-Scholes option pricing model.

The table presented below is a summary of changes in the fair value of the Company's Level 3 valuations for the warrant liability and SARs liability for the period ended September 30, 2016:

	Level 3 liabilities	
	Warrants	SARs
Beginning balance as of December 31, 2015	$ 48	$ —
Change in fair value	(44)	838
Ending balance as of September 30, 2016	$ 4	$ 838

Fair value of the warrant liability is estimated using an option-pricing model, which includes variables such as the expected volatility based on guideline public companies, the stock fair value, and the estimated time to a liquidity event. The significant assumptions used in preparing the option pricing model for valuing the Company's warrants as of September 30, 2016 include (i) volatility (68%—75%), (ii) risk free interest rate (0.52%—0.88%), (iii) strike price ($128.00-$2,520.00), (iv) fair value of common stock ($14.01), and (v) expected life (0.71—2.98 years). The significant assumptions used in preparing the option pricing model for valuing the Company's warrants as of December 31, 2015 include (i) volatility (62%-70%), (ii) risk free interest rate (0.86%—1.54%), (iii) strike price ($128.00—$2,520.00), (iv) fair value of common stock ($32.40), and (v) expected life (1.50—3.70 years).

Fair value of the SARs liability is estimated using an option-pricing model, which includes variables such as the expected volatility based on guideline public companies, the stock fair value, and the estimated time to a liquidity event. The significant assumptions used in preparing the option pricing model for valuing the Company's SARs as of September 30, 2016 include (i) volatility (69%—75%), (ii) risk free interest rate (0.29%—0.88%), (iii) strike price ($6.76-$30.86), (iv) fair value of common stock ($14.01), and (v) expected life (0.26—3.26 years).

4. Other comprehensive income (loss) and accumulated other comprehensive items

Other comprehensive income (loss) includes changes in equity that are excluded from net income (loss), such as unrealized gains and losses on marketable securities.

The following tables summarize other comprehensive income (loss) and the changes in accumulated other comprehensive items for the three and nine months ended September 30, 2016:

	Unrealized Gains/(Losses) On Marketable Securities, net of tax	Foreign Currency Translation	Total Accumulated Other Comprehensive Items
Balance at June 30, 2016	$ 29	$ 856	$ 885
Other comprehensive (loss) income before reclassifications	(189)	60	(129)
Amounts reclassified from other comprehensive items	—	—	—
Other comprehensive (loss) income	(189)	60	(129)
Balance at September 30, 2016	$ (160)	$ 916	$ 756

	Unrealized Gains/(Losses) On Marketable Securities, net of tax	Foreign Currency Translation	Total Accumulated Other Comprehensive Items
Balance at December 31, 2015	$ (589)	$ (611)	$ (1,200)
Other comprehensive income before reclassifications	429	1,527	1,956
Amounts reclassified from other comprehensive items	—	—	—
Other comprehensive income	429	1,527	1,956
Balance at September 30, 2016	$ (160)	$ 916	$ 756

5. Accounts payable and accrued expenses

Accounts payable and accrued expenses at September 30, 2016 and December 31, 2015 consist of the following:

	September 30, 2016	December 31, 2015
Employee compensation, benefits, and related accruals	$ 8,898	$ 11,187
Consulting and contracted research	13,336	13,753
Professional fees	1,679	2,523
Accounts payable	19,238	11,940
Accrued severance	231	—
Other	4,377	5,844
	$ 47,759	$ 45,247

6. Warrants

All of the Company’s outstanding warrants were classified as liabilities as of September 30, 2016 and December 31, 2015 because they contained non-standard antidilution provisions.

The following is a summary of the Company’s outstanding warrants as of September 30, 2016 and December 31, 2015:

	Warrant shares	Exercise price	Expiration
Common stock	6,250	$ 128.00	2017
Common stock	7,030	$ 128.00	2019
Common stock	130	$ 2,520.00	2019

7. Net loss per share

Basic earnings per share is computed by dividing net income (loss) by the weighted-average number of common shares outstanding. Diluted earnings per share is computed by dividing net income (loss) by the weighted-average number of common shares plus the effect of dilutive potential common shares outstanding during the period.

The following tables set forth the computation of basic and diluted net loss per share:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2016	2015	2016	2015
Numerator				
Net loss	$ (35,167)	$ (43,223)	$ (115,314)	$ (119,499)
Denominator				
Denominator for basic and diluted net loss per share	34,088,741	33,908,853	34,002,952	33,528,833
Net loss per share:				
Basic and diluted	$ (1.03) *	$ (1.27) *	$ (3.39) *	$ (3.56) *

*In the three and nine months ended September 30, 2016 and 2015, the Company experienced a net loss and therefore did not report any dilutive share impact.

The following table shows historical dilutive common share equivalents outstanding, which are not included in the above historical calculation, as the effect of their inclusion is anti-dilutive during each period.

	As of September 30,	
	2016	2015
Stock Options	5,832,166	4,788,264
Unvested restricted stock awards and units	272,579	353,135
Total	6,104,745	5,141,399

8. Stock award plan

On March 5, 2013, the Company's Board of Directors approved the 2013 Stock Incentive Plan, which provides for the granting of stock option awards, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards in the aggregate of 739,937 shares of common stock. On March 5, 2013, the Board approved a grant of 735,324 shares of restricted stock and 4,613 stock options. There are no additional shares available for issuance under this plan.

In May 2013, the Company's Board of Directors and stockholders increased by 2,500,000 the number of shares authorized under the 2009 Equity and Long Term Incentive Plan, which provides for the granting of stock option awards, restricted stock awards, and other stock-based and cash-based awards.

In May 2013, the Company's Board of Directors and stockholders approved the 2013 Long Term Incentive Plan, which became effective upon the closing of the Company's IPO. The 2013 Long Term Incentive Plan provides for the grant of incentive stock options, nonstatutory stock options, restricted stock awards and other stock-based awards. The number of shares of common stock reserved for issuance under the 2013 Long Term Incentive Plan is the sum of (1) 122,296 shares of common stock available for issuance under the Company's 2009 Equity and Long Term Incentive Plan and 2013 Stock Incentive Plan, (2) the number of shares (up to 3,040,444 shares) equal to the sum of the number of shares of common stock subject to outstanding awards under the Company's 1998 Employee, Director and Consultant Stock Option Plan, 2009 Equity and Long Term Incentive Plan and 2013 Stock Incentive Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right plus (3) an annual increase, to be added on the first day of each fiscal year until the expiration of the 2013 Long Term Incentive Plan, equal to the lowest of 2,500,000 shares of common stock, 4% of the number of shares of common stock outstanding on the first day of the fiscal year and an amount determined by the Company's Board of Directors. As of September 30, 2016, awards for 345,719 shares of common stock are available for issuance.

From January 1, 2016 through September 30, 2016, the Company issued a total of 1,440,445 stock options to various employees. Of those, 116,000 were inducement grants for non-statutory stock options. The inducement grant awards were

made pursuant to the NASDAQ inducement grant exception as a material component of our new hires' employment compensation and not under the 2013 Long Term Incentive Plan.

A summary of stock option activity is as follows:

	Number of options	Weighted-average exercise price	Weighted-average remaining contractual term	Aggregate intrinsic value
				(in thousands)
Outstanding at December 31, 2015	4,826,477	$ 37.20		
Granted	1,440,445	$ 28.55		
Exercised	(85,325)	$ 10.85		
Forfeited/Cancelled	(349,431)	$ 46.77		
Outstanding at September 30, 2016	5,832,166	$ 35.03	8.01 years	$ 4,132
Vested or Expected to vest at September 30, 2016	3,032,483	$ 35.79	8.50 years	$ 1,200
Exercisable at September 30, 2016	2,613,982	$ 34.08	7.38 years	$ 2,867

The fair value of grants made in the nine months ended September 30, 2016 was contemporaneously estimated on the date of grant using the following assumptions:

	Nine months ended September 30, 2016
Risk-free interest rate	1.30% — 2.24%
Expected volatility	67%—78%
Expected term	5.05– 10.00 years

The Company assumed no expected dividends for all grants. The weighted average grant date fair value of options granted during the nine month period ended September 30, 2016 was $17.67 per share.

The Company uses the "simplified method" to determine the expected term of options. Under this method, the expected term represents the average of the vesting period and the contractual term. The expected volatility of share options was estimated based on a historical volatility analysis of peers that were similar to the Company with respect to industry, stage of life cycle, size, and financial leverage. The risk-free rate of the option is based on U.S. Government Securities Treasury Constant Maturities yields at the date of grant for a term similar to the expected term of the option.

Restricted Stock Awards—Restricted stock awards are granted subject to certain restrictions, including in some cases service or time conditions (restricted stock). The grant-date fair value of restricted stock awards, which has been determined based upon the market value of the Company's shares on the grant date, is expensed over the vesting period.

Restricted Stock Units—Restricted stock units are granted subject to certain restrictions, including in some cases service or time conditions (restricted stock). The grant-date fair value of restricted stock units, which has been determined based upon the market value of the Company's shares on the grant date, is expensed over the vesting period.

The following table summarizes information on the Company's restricted stock awards and units:

	Restricted Stock Awards and Units	
	Number of Shares	Weighted Average Grant Date Fair Value
January 1, 2016	344,335	$ 10.85
Granted	141,185	$ 30.86
Vested	(163,635)	$ 10.85
Forfeited	(49,306)	$ 18.69
Unvested at September 30, 2016	272,579	$ 19.80

Stock Appreciation Rights—Stock appreciation rights (SARs) entitle the holder to receive, upon exercise, an amount of the Company's common stock or cash (or a combination thereof) determined by reference to appreciation, from and after the date of grant, in the fair market value of a share of the Company's common stock over the measurement price based on the exercise date.

In May 2016, a total of 897,290 SARs were granted to non-executive employees (the 2016 SARs). The 2016 SARs will vest annually in equal installments over four years and will be settled in cash on each vest date, requiring the Company to remeasure the SARs at each reporting period until vesting occurs. For the period ending September 30, 2016, the Company recorded $0.8 million in compensation expense related to the 2016 SARs.

Employee Stock Purchase Plan—In June 2016, the Company established an Employee Stock Purchase Plan (“ESPP” or “the Plan”) for certain eligible employees. The Plan is administered by the Company’s Board of Directors or a committee appointed by the Board. The total number of shares available for purchase under the Plan is one million shares of the Company’s common stock. Employees may participate over a six-month period through payroll withholdings and may purchase, at the end of the six-month period, the Company’s common stock at a purchase price of at least 85% of the closing price of a share of the Company’s common stock on the first business day of the offering period or the closing price of a share of the Company’s common stock on the last business day of the offering period, whichever is lower. No participant will be granted a right to purchase the Company’s common stock under the Plan if such participant would own more than 5% of the total combined voting power of the Company or any subsidiary of the Company after such purchase. For the period ending September 30, 2016 , the Company recorded $0.1 million in compensation expense related to the ESPP.

The Company recorded share-based compensation expense in the statement of operations related to incentive stock options, nonstatutory stock options, restricted stock awards, restricted stock units and the ESPP as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2016	2015	2016	2015
Research and development	$ 4,319	$ 3,828	$ 12,734	$ 12,452
Selling, general and administrative	4,640	4,226	13,876	13,678
Total	$ 8,959	$ 8,054	$ 26,610	$ 26,130

As of September 30, 2016 there was approximately $70.8 million of total unrecognized compensation cost related to unvested share-based compensation arrangements granted under the 2009 Equity and Long Term Incentive Plan, the 2013 Long Term Incentive Plan and equity awards made pursuant to the NASDAQ inducement grant exception for new hires. This cost is expected to be recognized as share-based compensation expense over the weighted average remaining service period of approximately 2.32 years.

9. Convertible Senior Notes

In August 2015, the Company issued, at par value, $150.0 million aggregate principal amount of 3.0% convertible senior notes due 2022 (the Convertible Notes). The Convertible Notes bear cash interest at a rate of 3.0% per year, payable semi-annually on February 15 and August 15 of each year, beginning on February 15, 2016. The Convertible Notes will mature on August 15, 2022, unless earlier repurchased or converted. The net proceeds to the Company from the offering were $145.4 million after deducting the initial purchasers’ discounts and commissions and the offering expenses payable by the Company.

The Convertible Notes are governed by an indenture (the Convertible Notes Indenture) with U.S Bank National Association as trustee (the Convertible Notes Trustee).

Holders may convert their Convertible Notes at their option at any time prior to the close of business on the business day immediately preceding February 15, 2022 only under the following circumstances:

- during any calendar quarter commencing on or after September 30, 2015 (and only during such calendar quarter), if the last reported sale price of the Company’s common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day;

- during the five business day period after any five consecutive trading day period (the “measurement period”) in which the trading price (as defined in the Convertible Notes Indenture) per $1,000 principal amount of Convertible Notes for

each trading day of the measurement period was less than 98% of the product of the last reported sale price of the Company's common stock and the conversion rate on each such trading day;

- during any period after the Company has issued notice of redemption until the close of business on the scheduled trading day immediately preceding the relevant redemption date; or

- upon the occurrence of specified corporate events

On or after February 15, 2022, until the close of business on the business day immediately preceding the maturity date, holders may convert their Convertible Notes at any time, regardless of the foregoing circumstances. Upon conversion, the Company will pay cash up to the aggregate principal amount of the Convertible Notes to be converted and deliver shares of its common stock in respect of the remainder, if any, of its conversion obligation in excess of the aggregate principal amount of Convertible Notes being converted.

The conversion rate for the Convertible Notes was initially, and remains, 17.7487 shares of the Company's common stock per $1,000 principal amount of the Convertible Notes, which is equivalent to an initial conversion price of approximately $56.34 per share of the Company's common stock.

The Company may not redeem the Convertible Notes prior to August 20, 2018. The Company may redeem for cash all or any portion of the Convertible Notes, at its option, on or after August 20, 2018 if the last reported sale price of its common stock has been at least 130% of the conversion price then in effect on the last trading day of, and for at least 19 other trading days (whether or not consecutive) during, any 30 consecutive trading day period ending on, and including, the trading day immediately preceding the date on which the Company provides notice of redemption, at a redemption price equal to 100% of the principal amount of the Convertible Notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date. No sinking fund is provided for the Convertible Notes, which means that the Company is not required to redeem or retire the Convertible Notes periodically.

If the Company undergoes a "fundamental change" (as defined in the Indenture governing the Convertible Notes Indenture), subject to certain conditions, holders of the Convertible Notes may require the Company to repurchase for cash all or part of their Convertible Notes at a repurchase price equal to 100% of the principal amount of the Convertible Notes to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date.

The Convertible Notes Indenture contains customary events of default with respect to the Convertible Notes, including that upon certain events of default (including the Company's failure to make any payment of principal or interest on the Convertible Notes when due and payable) occurring and continuing, the Convertible Notes Trustee by notice to the Company, or the holders of at least 25% in principal amount of the outstanding Convertible Notes by notice to the Company and the Convertible Notes Trustee, may, and the Convertible Notes Trustee at the request of such holders (subject to the provisions of the Convertible Notes Indenture) shall, declare 100% of the principal of and accrued and unpaid interest, if any, on all the Convertible Notes to be due and payable. In case of certain events of bankruptcy, insolvency or reorganization, involving the Company or a significant subsidiary, 100% of the principal of and accrued and unpaid interest on the Convertible Notes will automatically become due and payable. Upon such a declaration of acceleration, such principal and accrued and unpaid interest, if any, will be due and payable immediately.

The Company accounts for the Convertible Notes as a liability and equity component where the carrying value of the liability component will be valued based on a similar instrument. In accounting for the issuance of the Convertible Notes, the Company separated the Convertible Notes into liability and equity components. The carrying amount of the liability component was calculated by measuring the fair value of a similar liability that does not have an associated convertible feature. The carrying amount of the equity component representing the conversion option was determined by deducting the fair value of the liability component from the par value of the Convertible Notes as a whole. The excess of the principal amount of the liability component over its carrying amount, referred to as the debt discount, is amortized to interest expense over the seven-year term of the Convertible Notes. The equity component is not re-measured as long as it continues to meet the conditions for equity classification.

In accounting for the transaction costs related to the issuance of the Convertible Notes, the Company allocated the total costs incurred to the liability and equity components of the Convertible Notes based on their relative values. Transaction costs attributable to the liability component are amortized to interest expense over the seven-year term of the Convertible Notes, and transaction costs attributable to the equity component are netted with the equity components in stockholders' equity. Additionally, the Company initially recorded a net deferred tax liability of $22.3 million in connection with the Notes.

The Convertible Notes consist of the following:

Liability component	September 30, 2016	December 31, 2015
Principal	$ 150,000	$ 150,000
Less: Debt issuance costs	(2,536)	(2,760)
Less: Debt discount, net(1)	(50,905)	(55,392)
Net carrying amount	$ 96,559	$ 91,848

(1) Included in the consolidated balance sheets within convertible senior notes (due 2022) and amortized to interest expense over the remaining life of the Convertible Notes using the effective interest rate method.

The fair value of the Convertible Notes was approximately $89.2 million as of September 30, 2016. The Company estimates the fair value of its Convertible Notes utilizing market quotations for debt that have quoted prices in active markets. As of September 30, 2016, the remaining contractual life of the Convertible Notes is approximately 5.9 years.

The following table sets forth total interest expense recognized related to the Convertible Notes:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2016	2015	2016	2015
Contractual interest expense	$ 1,131	$ 584	$ 3,372	$ 584
Amortization of debt issuance costs	77	37	224	37
Amortization of debt discount	1,546	736	4,487	736
Total	$ 2,754	$ 1,357	$ 8,083	$ 1,357
Effective interest rate of the liability component	11%	11%	11%	11%

10. Restructuring

In March 2016, the Company commenced implementation of a reorganization of its operations intended to improve efficiency and better align the Company's costs and employment structure with its strategic plans. The Company completed its reorganization in June 2016 and recorded a one-time charge of $2.5 million for the nine month period ended September 30, 2016. The total $2.5 million in one-time charges is related to work-force reduction, recorded in research and development and selling, general and administrative expenses in the accompanying statement of operations.

	Balance as of June 30, 2016	Expenses, net	Cash	Balance as of September 30, 2016
2016 workforce reduction	$ 995	$ 33	$ (797)	$ 231

11. Commitments and contingencies

Under various agreements, the Company will be required to pay royalties and milestone payments upon the successful development and commercialization of products. The Company has entered into funding agreements with The Wellcome Trust Limited (Wellcome Trust) for the research and development of small molecule compounds. To the extent that the Company develops and commercializes program intellectual property on a for-profit basis, it may become obligated to pay to Wellcome Trust development and regulatory milestone payments of up to an aggregate of $68.9 million and single-digit royalties on sales of any research program product. The Company's obligation to pay such royalties would continue on a country-by-country basis until the longer of the expiration of the last patent in the program intellectual property in such country covering the research program product and the expiration of market exclusivity of such product in such country. The Company's first such milestone payment of $0.8 million payable to Wellcome Trust occurred in the second quarter of 2016.

The Company has also entered into a collaboration agreement with the SMA Foundation. The Company may become obligated to pay the SMA Foundation single- digit royalties on worldwide net product sales of any collaboration product that we successfully develop and subsequently commercialize or, if we outlicense rights to a collaboration product, a specified percentage of certain payments we receive from our licensee. The Company is not obligated to make such payments unless and until annual sales of a collaboration product exceed a designated threshold. The Company's obligation to make such payments would end upon our payment to the SMA Foundation of a specified amount.

The Company has employment agreements with certain employees which require the funding of a specific level of payments, if certain events, such as a change in control or termination without cause, occur.

12. Subsequent events

The Company has evaluated all subsequent events and transactions through the filing date. There were no material events that impacted the unaudited consolidated financial statements or disclosures.

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

The following discussion of our financial condition and results of operations should be read in conjunction with our financial statements and the notes to those financial statements 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, 2015 included in our Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 29, 2016. This discussion contains forward-looking statements that involve significant risks and uncertainties. As a result of many factors, such as those set forth in Part II, Item 1A. (Risk Factors) of this Quarterly Report on Form 10-Q, our actual results may differ materially from those anticipated in these forward-looking statements.

Our Company

We are a global biopharmaceutical company focused on the discovery, development and commercialization of orally administered, small molecule therapeutics targeting an area of RNA biology we refer to as post-transcriptional control. We have discovered all of our compounds currently under development using our proprietary technologies. We plan to continue to develop these compounds both on our own and through selective collaboration arrangements with leading pharmaceutical and biotechnology companies. Our internally discovered pipeline addresses multiple therapeutic areas, including rare disorders and oncology.

During the quarter ended September 30, 2016, we recognized $22.0 million in sales of Translarna™ (ataluren), our lead product, for the treatment of nonsense mutation Duchenne muscular dystrophy, or nmDMD. Translarna is currently available in over 20 countries on a commercial basis or through a reimbursed early access program, or EAP. Translarna is an investigational new drug in the United States, or U.S. We hold worldwide commercialization rights to Translarna for all indications in all territories.

Corporate Updates

Regulatory, clinical and marketing authorization matters for Translarna in nonsense mutation Duchenne muscular dystrophy

United States. In October 2016, the Office of Drug Evaluation I of the U.S. Food and Drug Administration, or FDA, denied our first appeal of the Refuse to File letter issued by the FDA's Division of Neurological Products, or DNP, on February 22, 2016 regarding our New Drug Application, or NDA, for Translarna for the treatment of nmDMD.

We intend to escalate the appeal to the next supervisory level of the FDA. We anticipate that multiple cycles of appeal to progressively higher levels of the FDA may be required before resolution of this matter is achieved under the formal dispute resolution process. We currently expect that final conclusion of the appeal process could occur in the first half of 2017, subject to any determination we may make to pursue an alternate regulatory strategy for advancing the potential approval of Translarna for the treatment of nmDMD in the United States.

Our planned continuing appeal of the DNP's refusal to review our NDA is being conducted in accordance with the formal dispute resolution process that exists within the FDA's Center for Drug Evaluation and Research. The formal dispute resolution process exists to encourage open, prompt discussion of scientific and procedural disputes that arise during the drug development, new drug review, and post-marketing oversight processes of the FDA.

There is substantial risk, notwithstanding any dialogue we have had or any further dialogue we may be able to initiate with the FDA, pursuant to the ongoing formal dispute resolution process or otherwise, that the agency will continue to disagree with our interpretation of the results of ACT DMD and the totality of clinical data from our trials and we may be required to perform additional clinical and non-clinical trials or complete additional analyses in order to enable FDA review of an NDA submission. Any such requirement for additional trials prior to approval, or otherwise, would result in significant additional costs and would most likely result in our inability to sell Translarna in the United States for a significant period of time, if ever.

For important information with respect to risks related to our ability to obtain marketing authorization for Translarna for the treatment of nmDMD in the U.S., see "Item 1A. Risk Factors," including the risk factor titled, *"The FDA denied our first appeal of the Refuse to File letter we received from the agency regarding our NDA for Translarna for the treatment of nmDMD, there is substantial risk that we will not be successful in further appeals of the Refuse to File letter to progressively higher levels of the FDA, and by determining to continue to pursue our appeal under the formal dispute resolution process with the FDA, we have postponed other available strategic pathways which may have proven to be more effective. If there are delays in obtaining regulatory approval in the United States, we will not be able to commercialize Translarna for nmDMD in that territory and our ability to generate revenue will be materially impaired."*

European Economic Area. We received marketing authorization from the European Commission in August 2014 for Translarna for the treatment of nmDMD in ambulatory patients aged five years and older in the 31 member states of the European Economic Area, or EEA. The marketing authorization is subject to annual review and renewal by the European Commission following reassessment by the European Medicines Agency, or EMA, of the risk-benefit balance of continued authorization, which we refer to as the annual EMA reassessment, as well as our satisfaction of other conditions and obligations placed upon the marketing authorization.

In fulfillment of an initial condition to our marketing authorization, in January 2016 we submitted the final clinical study report from our Phase 3 ACT DMD trial to the EMA. We made this submission as a type II variation request that sought to have this initial condition to our marketing authorization removed and a full marketing authorization granted. In February 2016, we also submitted a marketing authorization renewal request with the EMA. As of the time of this filing, the EMA's Committee for Medicinal Products for Human Use, or CHMP, has not issued an opinion with respect to our 2016 request for annual marketing authorization renewal and the annual EMA reassessment process remains ongoing. While the EMA has not formally declined our type II variation request for full approval of our marketing authorization, we believe that it is unlikely that the EMA will recommend in favor of this request.

Over the last several months, we have been engaged in constructive discussions with the CHMP regarding our requests for continuation of the marketing authorization, including participation in an advice procedure and meeting with the Scientific Advice Working Party, a Scientific Advisory Group meeting, and an oral explanation meeting with the CHMP, during the second half of 2016.

Following conclusion of our October 2016 oral explanation meeting, the CHMP issued a request for supplemental information, or RSI, including a request classified as a major objection. As with prior RSIs we received during the marketing authorization renewal and variation request process, the major objection relates to the efficacy and overall risk-benefit profile of Translarna as well as the design and conduct of an additional clinical trial that would provide comprehensive clinical data. Generally speaking, a failure to adequately address a major objection would preclude a recommendation for renewal of a marketing authorization.

We have submitted our responses to the RSI and anticipate that we will participate in further interactions with the CHMP this year. The extended duration of this renewal cycle and some of the recent feedback we have received as part of the annual EMA reassessment process have introduced a greater degree of uncertainty as to whether we will receive a positive opinion from the CHMP.

We continue to believe that if the CHMP issues a positive opinion in favor of the renewal of Translarna's marketing authorization, such renewal, and any subsequent annual renewals, will be coupled with an obligation to conduct an agreed upon new clinical trial of Translarna for the treatment of nmDMD. However, the CHMP may issue a negative opinion against renewal of the marketing authorization on the basis that, in the committee's view, the balance of risks and benefits of using Translarna for the treatment of nmDMD has changed materially. In such an event the European Commission could, at the EMA's recommendation, vary, suspend, withdraw or refuse to renew the marketing authorization for Translarna.

Even if the CHMP determines to issue a positive opinion, the EMA may impose other new conditions to our marketing authorization (in addition to the potential clinical trial described above) and may make other recommendations, including new label restrictions. In the event that we do secure annual renewal of the marketing authorization, the EMA could nevertheless later determine that we have not complied, or are unable to comply, with any conditions that have been or may be placed on the marketing authorization, which again could result in the withdrawal of our marketing authorization or other outcome that would have a materially adverse effect on our business.

In the event that the EMA, through the CHMP, determines to issue a negative opinion to the European Commission recommending the withdrawal or refusal to renew Translarna's marketing authorization, we would have the right to request a

re-examination of the CHMP recommendation no later than 15 days after receipt of the CHMP opinion. The appeal procedure would allow us 60 days to submit grounds for appeal and the CHMP would then have 60 days to consider a revision of its initial opinion. We expect that our current marketing authorization would remain valid during any such appeal process. If an appeal is unsuccessful, we could resubmit a new application for marketing authorization in the EEA at a later date.

If our marketing authorization in the EEA is not renewed, or our product label is materially restricted, we would lose all, or a significant portion of, our ability to generate revenue from product sales, whether pursuant to a commercial or an EAP program and throughout all territories.

The RSI also includes requests categorized as other concerns, which do not rise to the level of a major objection, and are generally associated with long-term risk and labeling matters as well as the primary pharmacology of Translarna. For example, as previously disclosed, changes in blood pressure and lipid profile were observed in a proportion of the Translarna-treated patients in ACT DMD. While the CHMP notes in its assessment report that the safety profile of Translarna could be considered acceptable, it further notes that Translarna is intended to be used chronically in boys with nmDMD who typically already have compromised cardiac function and are also being treated with corticosteroids that generally leads to increased blood pressure and lipid changes. As a result, we have been asked to discuss these topics in our Risk Management Plan and to propose relevant pharmacovigilance activities to collect further data regarding potential long term cardiovascular effects. The current warnings and precautions section of our approved Summary of Product Characteristics, or product label for Translarna, already notes that lipid levels and blood pressure should be monitored on a regular basis.

We anticipate that an opinion regarding our marketing authorization renewal request will be adopted by the CHMP before the end of 2016. We expect that, pursuant to applicable regulations and as confirmed in writing by the EMA, our current marketing authorization status (which was last renewed by the European Commission in the third quarter of 2015) will remain valid while the annual EMA reassessment is ongoing and until it is concluded with an opinion from the European Commission with respect to renewal of our marketing authorization.

For additional information regarding the risks related to the renewal of our marketing authorization in the EEA, see “Item 1A. Risk Factors,” including the risk factor titled, “*Our marketing authorization in the EEA requires annual renewal by the European Commission, which, as of the date of this filing, has not been granted, and there is substantial risk that the EMA will not determine that the risk-benefit balance of Translarna supports renewal of our marketing authorization, on the current label, or at all, and, even if the European Commission grants renewal of our marketing authorization, such renewal will likely be conditioned upon the results of a not yet designed trial for Translarna for the treatment of nmDMD, which will likely result in significant expense and uncertainty for us. If we are not able to obtain renewal of our marketing authorization, we will not be able to continue to commercialize Translarna for nmDMD and our ability to generate revenue will be materially impaired.*”

Phase 2 Pediatric Study. As part of our ongoing commitments under our marketing authorization in the EEA and to support the potential expansion of Translarna’s label to younger patients, we initiated a Phase 2 pediatric clinical study of Translarna for the treatment of nmDMD in patients two to five years of age in June 2016. This Phase 2, open-label, multiple-dose study will evaluate the safety and pharmacokinetics of Translarna in pediatric patients and is ongoing.

Other territories. In March 2016, we withdrew our New Drug Submission, or NDS, with Health Canada for Translarna for nmDMD. We currently plan to resubmit the NDS with the results of the ACT DMD trial in 2017, subject to the outcome of the regulatory matters described above. Many territories outside of the EEA reference and depend on the determinations by the EMA when considering the grant of a marketing authorization. For example, while Translarna received marketing authorization for the treatment of nmDMD in Israel in August 2015 and South Korea in December 2015, maintenance of marketing authorization in these countries will depend on the renewal and approval by the EMA for Translarna in the EEA. In the event that the EMA determines not to renew or otherwise modifies or withdraws our marketing authorization in the EEA, we may not be able to maintain our marketing authorizations in these other territories.

Early Access Programs. We have been making Translarna for the treatment of nmDMD available through reimbursed early access programs, or EAP programs, in selected countries where funded named patient or cohort programs exist, both within the EEA and in other territories. All of these programs are supported by the EMA’s assessment of Translarna and our marketing authorization in the EEA. As of today, Translarna is available under EAP or similar styled programs in Argentina, Brazil, Canada, Colombia, Cyprus, France, Greece, Israel, Italy, Kuwait, Portugal, Spain, Sweden, Switzerland, and Turkey.

Commercial and market access matters for Translarna in nonsense mutation Duchenne muscular dystrophy

The biopharmaceutical industry, including PTC, has experienced significant pressure on pricing for pharmaceuticals and orphan drug pricing is also drawing significant attention. Government authorities and other third-party payors have attempted to

control costs by limiting coverage and the amount of reimbursement for particular medications. Prices at which we or our customers seek reimbursement for our products can be subject to challenge, reduction or denial by the government and other payers. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. In addition, the price that is approved by local governmental authorities pursuant to commercial pricing and reimbursement processes may be significantly lower than the price charged for purchases of product in that country pursuant to a reimbursed early access program.

In some countries, such as France and Germany, EAP and commercial sales of a product can begin while pricing and reimbursement rates are under discussion with the applicable government health authorities. In the event that the negotiated price of the product is lower than the amount reimbursed for sales made prior to the conclusion of price negotiations, the company may become obligated to repay such excess amount to the applicable government health program. In certain countries, we record revenue net of estimated government and other third party discounts and rebates which will be finalized in the future. Allowances are recorded as a reduction of gross revenue at the time revenues from product sales are recognized. Our allowances may be adjusted over time to reflect known changes in factors which may impact revenue recognition in any given quarter.

Each country, including each member state of the EEA, has its own pricing and reimbursement regulations and many countries have other regulations related to the marketing and sale of pharmaceutical products in the applicable country. The pricing and reimbursement process varies from country to country and can take over 18 months from initiation to completion. As a result, our commercial launch will continue to be on a country-by-country basis. We generally will not be able to commence commercial sales of Translarna for the treatment of nmDMD pursuant to our marketing authorization in the EEA in any particular member state of the EEA until we conclude the applicable pricing and reimbursement negotiations and comply with any licensing, employment or related regulatory requirements in that country.

During the third quarter of 2016, Translarna became available to patients in England following the issuance of final guidance by the National Institute for Health and Care Excellence, or NICE, recommending Translarna for nmDMD patients within the EMA-approval label when used in connection with a five-year managed access agreement. The managed access agreement between us, NICE, NHS England and other interested parties establishes the clinical and commercial details surrounding the use of Translarna in England, including the terms and conditions of a confidential financial arrangement and the collection of further data on the efficacy of Translarna for the treatment of nmDMD over a five-year period with NICE guidance to be reviewed again at the end of that period, before future funding decisions are taken.

In addition to the United Kingdom, final commercial reference pricing for Translarna is currently available in Austria, Czech Republic, Denmark, Hungary, Norway, and Slovakia. In Italy, we recently reached a successful conclusion to pricing and reimbursement negotiations, with terms expected to be effective in January 2017. While we have submitted pricing and reimbursement dossiers with respect to Translarna for the treatment of nmDMD in other key EEA countries, we have only received both pricing and reimbursement approval on terms that are acceptable to us in a limited number of countries. For example, we determined to delist Translarna from the German pharmacy ordering system, effective April 1, 2016, after we were unable to achieve an acceptable agreement on pricing and reimbursement terms with the German Federal Association of the Statutory Health Insurances. It is our understanding that the majority of applicable patients and healthcare professionals in Germany have begun to access Translarna through a reimbursed importation pathway possible under German law. For any sales made directly in Germany from local pharmacies since December 2015, we are required to reimburse German payors the difference between the commercial price of Translarna in Germany and the price established by the German arbitration board. Any sales made to German patients via the reimbursed importation pathway are not subject to this arbitration price.

We expect that net product sales will fluctuate quarter-over-quarter. In some countries, including Brazil, orders for named patient sales are for multiple months of therapy which can lead to an unevenness in orders. Other factors may also contribute to fluctuations in quarterly net product sales including Translarna’s availability in any particular territory, government actions, economic pressures, political unrest and other factors.

Net product sales in general are impacted by many factors such as the timing of decisions by regulatory authorities, in particular the FDA and the EMA with respect to our ability to market or sell Translarna for the treatment of nmDMD, and our ability to successfully negotiate favorable pricing and reimbursement processes on a timely basis in the countries in which we have or may obtain regulatory approval, including the United States, EEA and other territories. In addition, if we are able to reach agreement with European regulators on a new clinical trial of Translarna for the treatment of nmDMD, we may enroll patients in countries where Translarna is currently available on a reimbursed basis, which could impact growth in our net product sales.

For important information regarding risks to our business arising as a result matters relating to pharmaceutical pricing and reimbursement see “Item 1A. Risk Factors,” including the risk factor titled “*Our initial commercial launch of Translarna has begun in, and is expected to continue to take place in, countries that tend to impose strict price controls, which may adversely affect our revenues, if any. Failure to obtain and maintain acceptable pricing and reimbursement terms for Translarna in the European Economic Area and other jurisdictions would prevent us from marketing our products in such regions*.”

Prevalence estimates for rare diseases are typically provided in ranges due to the uncertainties associated with the methodologies used to derive estimates such as epidemiology assumptions. It can take many years of experience in rare disease market places before prevalence becomes well characterized. We are launching the first therapy specifically aimed at DMD patients and in particular DMD patients with nonsense mutation. Our experience to date suggests that there may be up to 7,000 nmDMD patients globally and that approximately 40% of such patients are qualified for treatment under our current product label in the EEA. Country specific epidemiology will continue to be refined and characterized over the coming years and we have determined that we are not able to provide or confirm prior prevalence estimates on a country or regional basis at this time. Our estimates of both the number of people who have DMD caused by a nonsense mutation, as well as the subset of people with nmDMD who are ambulatory and at least five years old, are based on our beliefs and estimates derived from a variety of sources and may prove to be incorrect. Prevalence estimates vary given some degree of variation in the incidence of live male births, the incidence of DMD, the incidence nonsense mutations and other factors.

Translarna™ for nonsense mutation cystic fibrosis

We anticipate top-line results from our global, confirmatory Phase 3 clinical trial of Translarna for the treatment of cystic fibrosis caused by nonsense mutations, or nmCF, toward the end of the first quarter of 2017. We refer to this trial as ACT CF.

During the third quarter of 2016, we solicited feedback from the FDA (via a Type C meeting) and our CHMP rapporteurs on proposed revisions to our clinical trial protocol and the impact of such proposed revisions on the statistical analysis plan, or SAP, for ACT CF. Following receipt of feedback from these regulators, we amended the protocol to change the primary endpoint from relative change in percent of predicted forced expiratory volume in one second, or %-predicted FEV_1, at week 48 to absolute change in %-predicted FEV_1 assessed as an average at Week 40 and at Week 48. %-predicted FEV_1 is based on a comparison to healthy individuals matched for age, height and gender. The change in primary endpoint was largely driven by prior feedback we received from the FDA and the EMA on the trial design of ACT CF, as well as precedents with respect to the more recent approvals of cystic fibrosis-related therapies. Under this revision, data for relative change in %-predicted FEV_1 compared to placebo will be provided as supportive analysis to the primary endpoint. This change of primary endpoint to measure absolute change in %-predicted FEV_1 does not impact the statistical power of ACT CF.

In addition to the FDA's 2016 feedback with respect to the change in the primary endpoint, the agency provided further feedback at the same time regarding elements of our clinical trial protocol which we believe indicate the FDA’s willingness to accept and review a future application based on the results from ACT CF, provided that the revised primary and secondary endpoints provide strong evidence of effectiveness. As previously disclosed, we had interactions with the FDA in 2012 and 2013 with regards to our prior completed Phase 3 clinical trial of Translarna for the treatment of nmCF and our new clinical trial design. At that time, the FDA made certain key recommendations that we did not integrate into the trial. Specifically, the FDA recommended a three-year trial duration and the designation of FEV_1, CF pulmonary exacerbations, and body mass index, or BMI, as three co-primary endpoints for the trial. Our ACT CF protocol continues to specify FEV_1 as the primary endpoint and each of pulmonary exacerbations, change from baseline BMI in patients, and health-related quality of life (respiratory domain) as secondary endpoints. We believe that these endpoints are consistent with other recent and ongoing clinical trials in cystic fibrosis and our earlier discussions with the FDA.

In the written feedback received during the 2016 third quarter, while the FDA acknowledged that we specified FEV_1 as our sole primary endpoint, the agency noted that both statistically and clinically persuasive evidence from analyses of the primary and key secondary measures in ACT CF will be critical to support the effectiveness of Translarna, especially in the context of a single phase 3 study.

With respect to the FDA’s 2013 advice concerning study duration, we continue to believe that a three-year trial would have resulted in a number of complications that ultimately would have limited the feasibility of ACF CF as well as the robustness of the data and conclusions that could be drawn from the results. In the written feedback received during the 2016 third quarter, the FDA acknowledged that a 48-week trial may be of sufficient duration to demonstrate that Translarna improves FEV_1 versus placebo, while noting that this duration would likely not be sufficient to demonstrate that Translarna prevents FEV_1 decline compared to placebo.

In our 2016 protocol amendment, we also identified three pediatric subgroups we intend to analyze in ACT CF: less than 12 years of age versus 12 years of age and older, 6 to 11 years of age, and 12 to 17 years of age. While these subgroups are not statistically defined and ACT CF is not powered to detect a difference in treatment effect by age group, we will analyze the primary and key secondary efficacy endpoint (pulmonary exacerbations) for these groups in order to support our assessment of any difference in clinical outcomes and treatment effect compared to the study population as a whole. Our three stratification groups for ACT CF remain unchanged: patients less than 18 years of age versus 18 years of age and older, baseline %-predicted FEV_1, and inhaled antibiotic use.

During the third quarter of 2015, we submitted to the EMA a type II variation to our marketing authorization of Translarna in the EEA for the treatment of nmDMD, described above, to request approval of Translarna for the treatment of nmCF. Our variation submission was primarily based on the data from our prior Phase 3 clinical trial in nmCF completed in 2011, including post-hoc analyses of the results. We believe that the collective data from our prior Phase 3 trial, including retrospective and subgroup analyses that we have performed, provide strong support for concluding that Translarna was active and showed clinically meaningful improvements over placebo; however, the primary efficacy endpoint in the intent to treat, or ITT, population did not achieve statistical significance.

At its December 2015 meeting, the CHMP discussed the safety and efficacy of Translarna in nmCF patients as a whole and in a subgroup of patients without concomitant treatment with inhaled aminoglycosides and Translarna's potential for renal and urinary toxicity. At the meeting the CHMP adopted a request for supplementary information with respect to our variation submission and we have submitted our initial response. During the second quarter of 2016, we received additional requests for supplemental information from the CHMP with respect to our type II variation request, including requests characterized as major objections related to the efficacy and safety of Translarna for the treatment of nmCF. We are in the process of preparing our response to the CHMP's requests.

Approval of the variation to our marketing authorization will depend on the EMA's assessment of the relative benefits and risks of approval. If we are unable to demonstrate the required relative risk-benefit profile, it is likely that the EMA will not grant us a variation approving Translarna for the treatment of nmCF. Based on recent interactions with the CHMP, we believe that the results from our ongoing ACT CF trial may be required before the CHMP issues an opinion with respect to this type II variation request and we no longer expect final resolution of this matter in 2016.

Even if the variation is approved, we expect that the EMA will require us, as a post approval measure, to provide comprehensive clinical data from ACT CF to the EMA. In addition, such variation, if granted, will be subject to annual review and renewal by the European Commission following reassessment by the EMA of the risk-benefit balance of the authorization, unless and until we are granted full marketing authorization for our primary marketing authorization in the EEA for Translarna for the treatment of nmDMD.

In the event that the European Commission determines not to renew our primary marketing authorization in the EEA for Translarna for the treatment of nmDMD, we would be required to submit a separate marketing authorization application to the EMA and European Commission for approval of Translarna for the treatment of nmCF, which would significantly delay our ability to market and sell Translarna in the EEA, if ever.

Translarna™ extension studies for nmDMD and nmCF

Several open-label extension studies involving patients who participated in our prior trials for nmDMD and nmCF are ongoing at multiple sites across the United States, Europe, and other territories. The primary purpose of the extension studies is long-term safety evaluation of Translarna. We continue to incur significant expense in connection with their ongoing operation. In certain limited territories where Translarna is available via a commercial or EAP program, we have begun to wind down the studies and are investigating the potential impact that additional site closures may have on our research and development expense.

Translarna™ for additional indications

Based on its understood mechanism of action, we believe Translarna may have benefit in the treatment of patients with any genetic disorder that arises as a result of a nonsense mutation. We are pursuing proof of concept studies for Translarna in additional indications, including mucopolysaccharidosis type I caused by nonsense mutation, or nmMPS I, nonsense mutation aniridia, and nonsense mutation Dravet syndrome/CDKL5.

Spinal muscular atrophy program

Two compounds, RG7800 and RG7916, are currently in clinical development within the spinal muscular atrophy, or SMA, joint development program with F. Hoffman-La Roche Ltd and Hoffman-La Roche Inc., which we refer to collectively as Roche, and the Spinal Muscular Atrophy Foundation, or SMA Foundation.

In October 2016, a Phase 2 clinical study investigating the safety, tolerability and efficacy of RG7916 initiated in pediatric and adult type 2 and type 3 SMA patients. The Phase 2 study, called Sunfish, will take place in two parts, each of which will be double-blinded, placebo-controlled, and randomized. Part one of Sunfish is an exploratory dose-finding study in approximately 36 type 2 and type 3 SMA patients for a minimum of 12 weeks with the primary objective of evaluating the safety, pharmacokinetics, and pharmacodynamics of RG7916 in patients, and to select the dose for the second part of the study. The pivotal part two of Sunfish will be a confirmatory study in approximately 150 type 2 and type 3 SMA patients for up to 24 months with the primary objective of evaluating the efficacy of RG7916 compared to placebo, followed by an open-label extension study. Part two of Sunfish is expected to initiate in 2017 and would trigger a $20 million milestone payment to us from Roche.

A similarly designed two-part study, called Firefish, to evaluate RG7916 in type I SMA patients is expected to begin in the coming months. Part one of Firefish is expected to be an open-label, dose-escalation study in at least eight infants for a minimum of four weeks, with the primary objective of assessing the safety profile of RG7916 in infants and determining the dose for part two of the study. Part two of Firefish is expected to be an open-label, single-arm study in approximately 40 infants with type I SMA for 24 months with the primary objective of assessing the efficacy of RG7916 at the selected dose after 12 months of treatment. Part two of Firefish will be followed by an open-label extension study.

A Phase 1 study for RG7916 in healthy volunteers to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics completed earlier this year. Results indicate that RG7916 was well tolerated and treatment resulted in dose-dependent increases of full length SMN2 mRNA and decreases of SMN2 mRNA without exon 7 (SMND7), which may be interpreted as proof of mechanism in terms of the expected pharmacodynamic effect.

RG7800 was formerly the subject of a Phase 2 randomized, double blind, placebo controlled trial called Moonfish in adult and pediatric patients with SMA. Dosing in the Moonfish trial was suspended in April 2015 and the trial was placed on clinical hold to investigate a non-clinical safety finding observed in a longer term animal study. RG7800 remains a potential product candidate under the SMA program; however, the Moonfish trial is expected to be terminated during the fourth quarter of 2016. We and our collaboration partners expect to utilize data from completed and ongoing studies to continue to compare the profiles of the RG7800 and RG7916 compounds to determine the best path forward for our SMA program.

Cancer stem cell program

A Phase 1 first-in-human, dose-escalation safety and pharmacokinetic open-label clinical study for our product candidate, PTC596, in advanced cancer patients with solid tumors initiated in April 2015. Safety data to date from the ongoing Phase 1 study was recently presented at European Society for Medical Oncology Congress. We intend to continue clinical development of PTC596 during 2017.

Funding

Since 2015, our revenues have been primarily generated from sales of Translarna for the treatment of nmDMD in territories where we are permitted to distribute Translarna under our early access programs, or EAPs, and in countries in the EEA where we were able to obtain acceptable pricing and reimbursement terms.

To date, we have financed our operations primarily through our offering of 3.00% convertible senior notes due August 15, 2022, or the Convertible Notes offering, our public offerings of common stock in February 2014 and in October 2014, our initial public offering of common stock in June 2013, private placements of our preferred stock, collaborations, bank debt and convertible debt financings and grants and clinical trial support from governmental and philanthropic organizations and patient advocacy groups in the disease areas addressed by our product candidates.

As of September 30, 2016, we had an accumulated deficit of $708.3 million. We had a net loss of $115.3 million and $119.5 million for the nine months ended September 30, 2016 and 2015, respectively.

Our ongoing ability to generate revenue is almost entirely dependent upon our ability to maintain our marketing authorization in the EEA for Translarna for the treatment of nmDMD in ambulatory patients aged five years and older. We expect to incur significant costs in connection with our efforts to maintain our marketing authorization, which requires renewal by the European Commission on an annual basis following the annual EMA reassessment process. As of the time of this filing, our most recent request for marketing authorization renewal has not been granted and remains subject to the annual EMA

reassessment process. If our marketing authorization is not renewed, or our product label is materially restricted, we would lose all, or a significant portion of, our ability to generate revenue from product sales, whether pursuant to a commercial or an EAP program and throughout all territories.

In addition, we believe that it is likely that if the CHMP issues an opinion in favor of the renewal of Translarna's marketing authorization, such renewal, and any subsequent annual renewals, will be coupled with an obligation to conduct an agreed upon new clinical trial of Translarna for the treatment of nmDMD. Designing, enrolling, conducting and completing a clinical trial is a time-consuming, expensive and uncertain process that takes years to complete, and we expect that we will incur material ongoing costs related to the development of such a trial in the short-term, as well as the implementation of the trial in the longer term.

We also recently initiated a formal dispute resolution process with the FDA, seeking to reverse the agency's refusal to file our NDA for Translarna for the treatment of nmDMD. Our first appeal under this process did not result in a successful reversal of the Refuse to File determination and we believe multiple iterations of the appeal to progressively higher levels of the FDA may be required by us under this process. We may incur significant costs in connection with our efforts to resolve the matters set forth in the Refuse to File letter.

We anticipate that our expenses will further increase in connection with the expansion of our global infrastructure as we continue to establish an international presence and commercialize Translarna for the treatment of nmDMD, including sales and marketing, legal and regulatory, distribution and manufacturing and administrative and employee-based expenses. In addition to the foregoing, we expect to continue to incur significant costs in connection with our ongoing confirmatory Phase 3 ACT CF clinical trial and open label extension clinical trials of Translarna for the treatment of nmDMD and nmCF as well as our Phase 2 proof-of-concept studies for nmMPS I, nonsense mutation aniridia and nonsense mutation Dravet syndrome/CDKL5. We also expect to incur ongoing research and development expenses for our other product candidates, including our ongoing Phase 1 clinical study under our cancer stem cell program. In addition, we may incur substantial costs in connection with our efforts to advance our regulatory submissions, including those we have made or may make for Translarna for the treatment of nmCF, including in connection with our variation submission with the EMA, which seeks to include Translarna for the treatment of nmCF on our current marketing authorization in the EEA. We have begun seeking and intend to continue to seek marketing authorization for Translarna for the treatment of nmDMD in territories outside of the EEA and we may also seek marketing authorization for Translarna for other indications. These efforts may significantly impact the timing and extent of our commercialization expenses.

With respect to our outstanding Convertible Notes, cash interest payments are payable on a semi-annual basis in arrears, which will require total funding of $4.5 million annually. Furthermore, as a result of our initial public offering in June 2013, we have incurred and expect to continue to incur additional costs associated with operating as a public company. These costs include significant legal, accounting, investor relations and other expenses that we did not incur as a private company. Additionally, we could be forced to expend significant resources in the defense of the pending securities class action lawsuits brought against us and certain of our executives, as described under Part II, Item 1. Legal Proceedings in this Quarterly Report on Form 10-Q. See also, "*The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock and lawsuits against us and our officers and directors*" under Part II, Item 1A. Risk Factors - Risks Related to Our Common Stock.

We will need to generate significant revenues to achieve and sustain profitability, and we may never do so. Accordingly, we may need to obtain substantial additional funding in connection with our continuing operations. Adequate additional financing may not be available to us on acceptable terms, or at all. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or our commercialization efforts.

Financial operations overview

To date, our net product sales have consisted solely of sales of Translarna for the treatment of nmDMD in territories outside of the U.S. Our process for recognizing revenue is described below under "Critical accounting policies and significant judgments and estimates—Revenue recognition".

Roche and the SMA Foundation Collaboration. In November 2011, we entered into a license and collaboration agreement, or licensing agreement, with Roche and the SMA Foundation pursuant to which we are collaborating with Roche and the SMA Foundation to further develop and commercialize compounds identified under our spinal muscular atrophy program with the SMA Foundation. The research component of this agreement terminated effective December 31, 2014. The licensing agreement included a $30 million upfront payment made in 2011 which was recognized on a deferred basis over the research term, and the potential for up to $460 million in milestone payments and royalties on net sales.

In August 2013, we announced the selection of a development candidate. The achievement of this milestone triggered a $10.0 million payment to us from Roche, which we recorded as collaboration revenue for the year ended December 31, 2013.

In January 2014, we initiated a Phase 1 clinical program, which triggered a $7.5 million milestone payment to us from Roche which we recorded as collaboration revenue for the year ended December 31, 2014.

In November 2014, we announced that our joint development program in Spinal Muscular Atrophy (SMA) with Roche and the SMA Foundation (SMAF) has started a Phase 2 study in adult and pediatric patients. The achievement of this milestone triggered a $10.0 million payment to us from Roche which we recorded as collaboration revenue for the year ended December 31, 2014.

Grant revenue. From time to time, we receive grant funding from various institutions and governmental bodies. The grants are typically for early discovery research, and generally such grant programs last from two to five years.

Research and development expense

Research and development expenses consist of the costs associated with our research activities, as well as the costs associated with our drug discovery efforts, conducting preclinical studies and clinical trials, manufacturing development efforts and activities related to regulatory filings. Our research and development expenses consist of:

- external research and development expenses incurred under agreements with third-party contract research organizations and investigative sites, third-party manufacturing organizations and consultants;

- employee-related expenses, which include salaries and benefits, including share-based compensation, for the personnel involved in our drug discovery and development activities; and

- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, IT, human resources and other support functions, depreciation of leasehold improvements and equipment, and laboratory and other supplies.

We use our employee and infrastructure resources across multiple research projects, including our drug development programs. We track expenses related to our clinical programs and certain preclinical programs on a per project basis.

We expect our research and development expenses to increase in connection with our ongoing activities, particularly as we continue our confirmatory Phase 3 ACT CF trial and open label extension clinical trials of Translarna for the treatment of nmDMD and nmCF, our Phase 2 proof-of-concept study of Translarna in nmMPS I, nonsense mutation aniridia, and nonsense mutation Dravet syndrome/CDKL5, and our Phase 1 clinical study for PTC596 under our cancer stem cell program. In addition, we believe that it is likely that if the CHMP issues an opinion in favor of the renewal of Translarna's marketing authorization in the EEA, such renewal, and any subsequent annual renewals, will be coupled with an obligation to conduct an agreed upon new clinical trial of Translarna for the treatment of nmDMD. The timing and amount of these expenses will depend upon the outcome of these ongoing clinical trials and the costs associated with our planned clinical trials. The timing and amount of these expenses will also depend on the costs associated with potential future clinical trials of our product candidates and the related expansion of our research and development organization, regulatory requirements, advancement of our preclinical programs and product candidate manufacturing costs.

The following tables provide research and development expense for our most advanced principal product development programs, for the three and nine months ended September 30, 2016 and 2015.

	Three Months Ended September 30,	
	2016	2015
	(in thousands)	
Translarna (nmDMD, nmCF, nmMPS I, aniridia and Dravet)	$ 22,088	$ 19,600
Antibacterial	13	2,527
Cancer stem cell	1,689	1,736
Next generation nonsense readthrough	1,621	1,857
Other research and preclinical	5,985	4,920
Total research and development	$ 31,396	$ 30,640

	Nine months ended September 30,	
	2016	2015
	(in thousands)	
Translarna (nmDMD, nmCF, nmMPS I, aniridia and Dravet)	$ 66,133	$ 54,524
Antibacterial	171	7,542
Cancer stem cell	5,523	5,413
Next generation nonsense readthrough	5,577	5,958
Other research and preclinical	14,218	13,331
Total research and development	$ 91,622	$ 86,768

The successful development of our product and product candidates is highly uncertain. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- the costs, timing and outcome of our efforts to resolve the matters set forth in the Refuse to File letter we received from the FDA in connection with our NDA for Translarna for the treatment of nmDMD, whether pursuant to continued appeal under the formal dispute resolution process or otherwise;
- the costs, timing and outcome of the annual EMA reassessment related to renewal of our marketing authorization in the EEA for Translarna for the treatment of nmDMD, including whether the EMA determines that the risk-benefit balance of Translarna supports renewal of our marketing authorization in the EEA, on the current approved label, or at all and the design of any acceptable new clinical trial in nmDMD we may be able to develop with input from the EMA, if any;
- the scope, rate of progress and expense of our clinical trials and other research and development activities;
- the potential benefits of our product and product candidate over other therapies;
- our ability to market, commercialize and achieve market acceptance for any of our product candidates that we are developing or may develop in the future, including our ability to negotiate pricing and reimbursement terms acceptable to us and to obtain or maintain marketing authorizations we have or may receive from our product and product candidates;
- clinical trial results;
- the terms and timing of regulatory approvals; and
- the expense of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights.

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

Selling, general and administrative expense

Selling, general and administrative expenses consist primarily of salaries and other related costs for personnel, including share-based compensation expenses, in our executive, legal, business development, finance, accounting, information technology and human resource functions. Other selling, general and administrative expenses include facility-related costs not otherwise included in research and development expense; advertising and promotional expenses; costs associated with industry and trade shows; and professional fees for legal services, including patent-related expenses, accounting services, miscellaneous selling costs and finishing costs incurred to direct product to commercial use.

We expect that selling, general and administrative expenses will increase in future periods as a result of our continued efforts to establish an expanded international presence in Europe and other territories and our continued efforts to commercialize Translarna for the treatment of nmDMD, including increased payroll, expanded infrastructure, commercial operations, increased consulting, legal, accounting and investor relations expenses.

Interest (expense) income, net

Interest (expense) income, net consists of interest income earned on investments and interest expense from the Convertible Notes outstanding.

Critical accounting policies and significant judgments and estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with generally accepted accounting principles in the United States. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenues and expenses during the reporting periods. Actual results may differ from these estimates under different assumptions or conditions.

Revenue recognition

We recognize revenue when amounts are realized or realizable and earned. Revenue is considered realizable and earned when the following criteria are met: (1) persuasive evidence of an arrangement exists; (2) delivery has occurred or services have been rendered; (3) the price is fixed or determinable; and (4) collection of the amounts due are reasonably assured.

Net Product Sales

To date, our net product sales have consisted solely of sales of Translarna for the treatment of nmDMD in territories outside of the U.S. We began recognizing revenue for payments received under the reimbursed EAPs for Translarna in nmDMD patients in select countries in the third quarter of 2014. We have now established a pattern of collectability and, since January 2015, we recognize revenue from product sales when there is persuasive evidence that an arrangement exists, title to product and associated risk of loss has passed to the customer, the price is fixed or determinable, collectability is reasonably assured and we have no further performance obligations in accordance with Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") Subtopic 605-15, Revenue Recognition—Products.

We have recorded revenue on sales where Translarna is available either on a commercial basis or through a reimbursed EAP program. Orders for Translarna are generally received from hospital and retail pharmacies and, in some cases, one of our third-party partner distributors. Our third-party distributors act as intermediaries between us and end users and do not typically stock significant quantities of Translarna. The ultimate payor for Translarna is typically a government authority or institution or a third-party health insurer. Prior to January 1, 2015, we generally recognized revenue for these reimbursed EAP programs once the product was shipped on behalf of the government authority or institution on a cash basis if all other revenue recognition criteria had been met. Beginning in the first quarter of 2015, we are recognizing revenue for Translarna as product is shipped, as we have established a pattern of collectability.

We record revenue net of estimated third party discounts and rebates. Allowances are recorded as a reduction of revenue at the time revenues from product sales are recognized. Allowances for government and other third-party rebates and discounts are established or estimated at the time of delivery. These allowances are adjusted to reflect known changes in factors and may impact such allowances in the quarter those changes are known.

We expect that net product sales will fluctuate quarter-over-quarter. In some countries, including Brazil, orders for named patient sales are for multiple months of therapy which can lead to an unevenness in orders. Other factors may also contribute to fluctuations in quarterly net product sales including Translarna's availability in any particular territory, government actions, economic pressures, political unrest and other factors. Net product sales are impacted by factors, such as the timing of decisions by regulatory authorities, in particular the FDA and the EMA with respect to our ability to market or sell Translarna for the treatment of nmDMD, and our ability to successfully negotiate favorable pricing and reimbursement processes on a timely basis in the countries in which we have or may obtain regulatory approval, including the United States, EEA and other territories. In addition, if we are able to reach agreement with European regulators on a new clinical trial of Translarna for the treatment of nmDMD, we may enroll patients in countries where Translarna is currently available on a reimbursed basis, which could impact growth in our net product sales.

Collaboration and Grant Revenue

The terms of collaboration agreements typically include payments of one or more of the following: nonrefundable, upfront license fees; milestone payments; research funding; and royalties on future product sales. In addition, if applicable, we generate service revenue through collaboration and grant agreements that provide for fees for research and development services or additional payments upon achievement of specified events.

We evaluate all contingent consideration earned, such as a milestone payment, using the criteria as provided by the Financial Accounting Standards Board, or FASB, guidance on the milestone method of revenue recognition. At the inception of a collaboration arrangement, we evaluate if milestone payments are substantive. The criteria requires that (1) we determine if the milestone is commensurate with either its performance to achieve the milestone or the enhancement of value resulting from our activities to achieve the milestone; (2) the milestone be related to past performance; and (3) the milestone be reasonable relative to all deliverable and payment terms of the collaboration arrangement. If these criteria are met then the contingent milestones can be considered as substantive milestones and will be recognized as revenue in the period that the milestone is achieved. We recognize royalties as earned in accordance with the terms of various research and collaboration agreements. If not substantive, the contingent consideration is allocated to the existing units of accounting based on relative selling price and recognized following the same basis previously established for the associated unit of accounting.

We recognize reimbursements for research and development costs under collaboration agreements as revenue as the services are performed. We record these reimbursements as revenue and not as a reduction of research and development expenses as we have the risks and rewards as the principal in the research and development activities.

Our principal obligation under our grant agreements is to conduct the internal or external research in the specific field funded by the grant. We determine, through the grant's normal research process, which research and development projects to pursue. We recognize grant revenues as the research activities are performed. If the grant includes an upfront payment, we defer the amount and recognize it as revenue as the expenditures are incurred.

Inventories and Cost of Product Revenues

In 2014, we were notified that the European Commission granted marketing authorization for Translarna for the treatment of nmDMD in ambulatory patients aged five years and older. The conditional marketing authorization allows us to market Translarna for the treatment of nmDMD in the 31 member states of European Economic Area. Our launch in these countries is on a country by country basis. This marketing authorization is subject to annual review and renewal by the European Commission following reassessment by the European Medicines Agency, or EMA, of the risk benefit balance of the authorization, which we refer to as the annual EMA reassessment. In the third quarter of 2015, the EMA approved the annual renewal of the marketing authorization for Translarna for the treatment of nmDMD. The authorization was further conditioned on our submission of the final report, including additional efficacy and safety data, from ACT DMD and our ability to implement measures, including pharmacovigilance plans that are detailed in the risk management plan for Translarna that was submitted to EMA. In January 2016, we submitted the final ACT DMD report to the EMA. We made this submission as a type II variation request that sought to have this initial condition to our marketing authorization removed and a full marketing authorization granted. In February 2016, we also submitted a marketing authorization renewal request with the EMA. The annual EMA reassessment process related to our 2016 marketing authorization request is still ongoing and, as of the time of this filing, renewal has not been granted. We expect that the EMA's CHMP will adopt an opinion as to whether to renew our marketing authorization for Translarna for the treatment of nmDMD by the end of 2016. Pursuant to applicable regulations, we expect that our current marketing authorization status (which was last renewed by the European Commission in the third quarter of 2015) will remain valid while the 2016 annual EMA reassessment is ongoing and until it is concluded with an opinion from the European Commission with respect to renewal of the marketing authorization.

In the event that our marketing authorization renewal request is granted, we plan to seek to renew the marketing authorization on an annual basis until any further obligations or conditions that may be placed by the European Commission on the marketing authorization have been fulfilled and the approval is converted from a conditional approval into a full approval. If we fail to satisfy such further obligations or conditions, or if it is determined that the balance of risks and benefits of using Translarna changes materially, the European Commission could, at the EMA's recommendation, vary, suspend, withdraw or refuse to renew the marketing authorization for Translarna or require additional clinical trials.

There continues to be substantial risk that regulators could suspend or not renew our marketing authorization in the future. As such, as of the date of this filing, we have not capitalized inventory given the near term uncertainty with respect to the long term utilization of Translarna finished product for commercial use. Had we capitalized as inventory all of our Translarna product that is available for commercial sale on hand as of September 30, 2016, the value of that inventory would have been approximately $1.3 million. In addition, had we expensed the cost of Translarna product sold as a cost of sales, our gross profit margin would have been greater than 90%, which we believe is consistent with the cost of producing small molecule therapeutics for orphan drug diseases in the pharmaceutical industry. We will continue to assess the appropriateness of inventory capitalization based on the outcome of applicable regulatory determinations, including the pending CHMP opinion regarding the potential annual renewal of our marketing authorization in the EEA, which is expected to be issued in 2016 and followed by ratification by the European Commission in early 2017. In the event the CHMP issues a positive opinion regarding renewal of our marketing authorization, and the European Commission ratifies such determination, we would expect to capitalize inventory and commence the expensing of cost of goods sold.

Accrued expenses

As part of the process of preparing our financial statements, we are required to estimate accrued expenses. This process involves communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us. Examples of estimated accrued expenses include:

- fees paid to contract research organizations in connection with preclinical and toxicology studies and clinical trials;
- fees paid to investigative sites in connection with clinical trials;
- fees paid to contract manufacturers in connection with the production of clinical trial materials; and
- professional service fees.

Share-based compensation

We expect to grant additional stock options that will result in additional share-based compensation expense. We measure the cost of employee services received in exchange for an award of equity instruments based on the grant date fair value of the award. For service type awards, share-based compensation expense is recognized on a straight-line basis over the period during which the employee is required to provide service in exchange for the entire award. For awards that vest or begin vesting upon achievement of a performance condition, we estimate the likelihood of satisfaction of the performance condition and recognize compensation expense when achievement of the performance condition is deemed probable using an accelerated attribution model.

From January 1, 2016 through September 30, 2016, we issued a total of 1,440,445 stock options to various employees. Of those, 116,000 were non-statutory stock option inducement grants made pursuant to the NASDAQ inducement grant exception as a material component of our new hires' employment compensation. All other stock option grants were made under our 2013 Long Term Incentive Plan.

The fair value of options is calculated using the Black-Scholes option pricing model to determine the fair value of stock options on the date of grant based on key assumptions, such as expected volatility and expected term. As a new public company, we do not have sufficient history to estimate the volatility of our common stock price or the expected life of the options. We calculate expected volatility based on reported data for similar publicly traded companies for which historical information is available and will continue to do so until the historical volatility of our common stock is sufficient to measure expected volatility for future option grants.

The fair value of grants made in the nine months ended September 30, 2016 was contemporaneously estimated on the date of grant using the following assumptions:

	2016
Risk-free interest rate	1.30% — 2.24%
Expected volatility	67%—78%
Expected term	5.05– 10.00 years

We assumed no expected dividends for all grants. The weighted average grant date fair value of options granted during the nine month period ended September 30, 2016 was $17.67 per share.

We use the “simplified method” to determine the expected term of options. Under this method, the expected term represents the average of the vesting period and the contractual term. The expected volatility of share options was estimated based on a historical volatility analysis of peers that were similar to us with respect to industry, stage of life cycle, size, and financial leverage. The risk-free rate of the option is based on U.S. Government Securities Treasury Constant Maturities yields at the date of grant for a term similar to the expected term of the option.

Restricted Stock Awards—Restricted stock awards are granted subject to certain restrictions, including service conditions. The grant-date fair value of restricted stock awards, which has been determined based upon the market value of our common stock on the grant date, is expensed over the vesting period.

Restricted Stock Units—Restricted stock units are granted subject to certain restrictions, including in some cases service or time conditions (restricted stock). The grant-date fair value of restricted stock units, which has been determined based upon the market value of our common stock on the grant date, is expensed over the vesting period.

The following table summarizes information on our restricted stock awards and units:

	Restricted Stock Awards and Units	
	Number of Shares	Weighted Average Grant Date Fair Value
January 1, 2016	344,335	$ 10.85
Granted	141,185	$ 30.86
Vested	(163,635)	$ 10.85
Forfeited	(49,306)	$ 18.69
September 30, 2016	272,579	$ 19.80

Stock Appreciation Rights—Stock appreciation rights (SARs) entitle the holder to receive, upon exercise, an amount of our common stock or cash (or a combination thereof) determined by reference to appreciation, from and after the date of grant, in the fair market value of a share of our common stock over the measurement price based on the exercise date.

In May 2016, a total of 897,290 SARs were granted to non-executive employees (the 2016 SARs). The 2016 SARs will vest annually in equal installments over four years and will be settled in cash on each vest date, requiring us to remeasure the SARs at each reporting period until vesting occurs. For the period ending September 30, 2016, we recorded $0.8 million in compensation expense related to the 2016 SARs.

Employee Stock Purchase Plan—In June 2016, we established an Employee Stock Purchase Plan (“ESPP” or “the Plan”) for certain eligible employees. The Plan is administered by our Board of Directors or a committee appointed by the Board. The total number of shares available for purchase under the Plan is one million shares of our common stock. Employees may participate over a six-month period through payroll withholdings and may purchase, at the end of the six-month period, the our common stock at a purchase price of at least 85% of the closing price of a share of our common stock on the first business day of the offering period or the closing price of a share of our common stock on the last business day of the offering period, whichever is lower. No participant will be granted a right to purchase our common stock under the Plan if such participant would own more than 5% of the total combined voting power of us or one of our subsidiaries. For the period ending September 30, 2016, we recorded $0.1 million in compensation expense related to the ESPP.

We recorded share-based compensation expense in the statement of operations related to incentive stock options, nonstatutory stock options, restricted stock awards, restricted stock units and the ESPP as follows:

	Three months ended September 30,		Nine months ended September 30,	
	2016	2015	2016	2015
Research and development	$ 4,319	$ 3,828	$ 12,734	$ 12,452
Selling, general and administrative	4,640	4,226	13,876	13,678
Total	$ 8,959	$ 8,054	$ 26,610	$ 26,130

As of September 30, 2016 there was approximately $70.8 million of total unrecognized compensation cost related to unvested share-based compensation arrangements granted under the 2009 Equity and Long Term Incentive Plan, the 2013 Long Term Incentive Plan and equity awards made pursuant to the NASDAQ inducement grant exception for new hires. This cost is expected to be recognized as share-based compensation expense over the weighted average remaining service period of approximately 2.32 years.

Results of operations

Three months ended September 30, 2016 compared to three months ended September 30, 2015

The following table summarizes revenues and selected expense and other income data for the three months ended September 30, 2016 and 2015.

(in thousands)	Three Months Ended September 30,		Change 2016 vs. 2015
	2016	2015	
Net product revenue	$ 22,013	$ 9,772	$ 12,241
Collaboration and grant revenue	973	4	969
Research and development expense	31,396	30,640	756
Selling, general and administrative expense	23,654	21,368	2,286
Interest expense, net	(2,133)	(852)	(1,281)

Net product revenues. Net product revenues were $22.0 million for the three months ended September 30, 2016, an increase of $12.2 million, or 125%, from $9.8 million for the three months ended September 30, 2015 due to continued expansion of commercial access to Translarna for nonsense mutation DMD boys outside of the U.S. We have recorded revenue on sales where Translarna is available either on a commercial basis or through a reimbursed EAP program and typically paid for by a government authority or institution. Since January 1, 2015, we have recognized revenue for Translarna as product is shipped, given we have established a pattern of collectability.

Collaboration and grant revenues. Collaboration and grant revenues were $1.0 million for the three months ended September 30, 2016, an increase of $1.0 million from $0.0 million for the three months ended September 30, 2015. The increase was primarily due to the recognition of a development milestone related to a grant agreement.

Research and development expense. Research and development expense was $31.4 million for the three months ended September 30, 2016, an increase of $0.8 million, or 2%, from $30.6 million for the three months ended September 30, 2015. The increase resulted primarily from an increase in consulting expenses associated with our ongoing clinical trials.

Selling, general and administrative expense. Selling, general and administrative expense was $23.7 million for the three months ended September 30, 2016, an increase of $2.3 million, or 11%, from $21.4 million for the three months ended September 30, 2015. The increase resulted primarily from additional costs associated with commercial activities in support of the expanded commercial launch of Translarna across Europe and other regions.

Interest expense, net. Interest expense, net was $2.1 million for the three months ended September 30, 2016, an increase of $1.3 million, from $0.9 million, for the three months ended September 30, 2015. The increase in interest expense was

primarily due to current year interest expense recorded from the Convertible Notes partially offset by interest income from investments.

Income tax expense. Income tax expense was $0.2 million for the three months ended September 30, 2016 and $0.1 million for the three months ended September 30, 2015. We are subject to income taxes in the United States, although currently not a tax payer, and various foreign jurisdictions, and our foreign tax liabilities are largely dependent upon the distribution of pre-tax earnings among these different jurisdictions.

The income tax benefit for the three months ended September 30, 2016 differed from the amounts computed by applying the U.S. federal income tax rate of 34% to loss before tax expense as a result of the favorable amount of profit mix in foreign jurisdictions which have lower tax rates, as well as by having a full valuation allowance in jurisdictions where we have net operating losses. We review the expected annual effective income tax rate and make changes on a quarterly basis as necessary based on certain factors such as changes in forecasted annual operating income, changes to the actual and permanent book-to-tax differences, and changes resulting from the impact of tax law changes.

Nine months ended September 30, 2016 compared to nine months ended September 30, 2015

The following table summarizes revenues and selected expense and other income data for the nine months ended September 30, 2016 and 2015.

(in thousands)	Nine Months Ended September 30, 2016	2015	Change 2016 vs. 2015
Net product revenue	$ 56,328	$ 21,002	$ 35,326
Collaboration and grant revenue	1,186	3,030	(1,844)
Research and development expense	91,622	86,768	4,854
Selling, general and administrative expense	72,958	56,193	16,765
Interest (expense) income, net	(6,149)	170	(6,319)

Net product revenues. Net product revenues were $56.3 million for the nine months ended September 30, 2016, an increase of $35.3 million, or 168%, from $21.0 million for the nine months ended September 30, 2015 due to continued expansion of commercial access to Translarna for nonsense mutation DMD boys outside of the U.S. We have recorded revenue on sales where Translarna is available either on a commercial basis or through a reimbursed EAP program and typically paid for by a government authority or institution. Since January 1, 2015, we have recognized revenue for Translarna as product is shipped, given we have established a pattern of collectability.

Collaboration and grant revenues. Collaboration and grant revenues were $1.2 million for the nine months ended September 30, 2016, a decrease of $1.8 million, or 61%, from $3.0 million for the nine months ended September 30, 2015. The decrease was primarily due to the recognition of deferred revenue from Roche’s collaboration milestone payments to us in the 2015 period.

Research and development expense. Research and development expense was $91.6 million for the nine months ended September 30, 2016, an increase of $4.9 million, or 6%, from $86.8 million for the nine months ended September 30, 2015. The increase resulted primarily from an increase in clinical trial related expenses associated with our ongoing clinical trials, supply chain activities in support of the expanded commercial launch of Translarna and increased expenses in connection with our expanding clinical-stage pipeline.

Selling, general and administrative expense. Selling, general and administrative expense was $73.0 million for the nine months ended September 30, 2016, an increase of $16.8 million, or 30%, from $56.2 million for the nine months ended September 30, 2015. The increase resulted primarily from additional costs associated with commercial activities in support of the expanded commercial launch of Translarna across Europe and other regions.

Interest (expense) income, net. Interest expense, net was $6.1 million for the nine months ended September 30, 2016, an increase in expense of $6.3 million from interest income of $0.2 million for the nine months ended September 30, 2015. The increase in interest expense was primarily due to current year interest expense recorded from the Convertible Notes partially offset by interest income from investments.

Income tax expense. Income tax expense was $0.2 million for the nine months ended September 30, 2016 and $0.2 million for the nine months ended September 30, 2015. We are subject to income taxes in the United States, although currently not a tax payer, and various foreign jurisdictions, and our foreign tax liabilities are largely dependent upon the distribution of pre-tax earnings among these different jurisdictions.

The income tax expense for the nine months ended September 30, 2016 differed from the amounts computed by applying the U.S. federal income tax rate of 34% to loss before tax expense as a result of the favorable amount of profit mix in foreign jurisdictions which have lower tax rates, as well as by having a full valuation allowance in jurisdictions where we have net operating losses. We review the expected annual effective income tax rate and make changes on a quarterly basis as necessary based on certain factors such as changes in forecasted annual operating income, changes to the actual and permanent book-to-tax differences, and changes resulting from the impact of tax law changes.

Liquidity and capital resources

Sources of liquidity

Since inception, we have incurred significant operating losses.

As a growing commercial-stage biopharmaceutical company, we are engaging in significant commercialization efforts for Translarna for nmDMD while also devoting a substantial portion of our efforts on research and development programs related to Translarna and our other product candidates. Our ongoing ability to generate revenue is almost entirely dependent upon our ability to maintain our marketing authorization in the EEA for Translarna for the treatment of nmDMD in ambulatory patients aged five years and older. The marketing authorization requires annual renewal by the European Commission. As of the time of this filing, our most recent request for marketing authorization renewal has not been granted and remains subject to the annual EMA reassessment process. During 2016, we expect that our revenues will be primarily generated from sales of Translarna in territories where we are permitted to distribute Translarna under our EAP programs, and those countries, in particular in the EEA, where we are able to obtain pricing and reimbursement approval at acceptable levels.

We have historically financed our operations primarily through the issuance and sale of our common stock in public offerings, the private placements of our preferred stock, collaborations, bank debt, convertible debt financings and grants and clinical trial support from governmental and philanthropic organizations and patient advocacy groups in the disease areas addressed by our product candidates. We expect to continue to incur significant expenses and operating losses for at least the next several years. The net losses we incur may fluctuate significantly from quarter to quarter.

In August 2015, we closed a private offering of $150 million in aggregate principal amount of 3.00% convertible senior notes due 2022, or the Convertible Notes, including the exercise by the initial purchasers of an option to purchase an additional $25 million in aggregate principal amount of the Convertible Notes. The Convertible Notes bear cash interest payable on February 15 and August 15 of each year, beginning on February 15, 2016. The Convertible Notes are senior unsecured obligations of ours and will mature on August 15, 2022, unless earlier converted, redeemed or repurchased in accordance with their terms prior to such date. We received net proceeds from the offering of approximately $145.4 million, after deducting the initial purchasers' discounts and commissions and the estimated offering expenses payable by us.

Cash flows

As of September 30, 2016 we had cash, cash equivalents and marketable securities of $248.3 million.

The following table provides information regarding our cash flows and our capital expenditures for the periods indicated.

	Nine Months Ended September 30,	
(in thousands)	**2016**	**2015**
Cash provided by (used in):		
Operating activities	(90,247)	(94,005)
Investing activities	81,350	31,019
Financing activities	926	154,039

Net cash used in operating activities was $90.2 million for the nine months ended September 30, 2016 and $94.0 million for the nine months ended September 30, 2015. The net cash used in operating activities primarily relates to supporting clinical development and commercial activities.

Net cash provided by investing activities was $81.4 million for the nine months ended September 30, 2016 and $31.0 million for the nine months ended September 30, 2015. Cash provided by investing activities was related to the sale and redemption of marketable securities to fund operations.

Net cash provided by financing activities was $0.9 million for the nine months ended September 30, 2016 and $154.0 million for the nine months ended September 30, 2015. The decrease in net cash provided by financing activities was attributable to the $150 million Convertible Notes offering in 2015.

Funding requirements

We expect to incur significant costs in connection with our efforts to maintain our marketing authorization for Translarna for the treatment of nmDMD in the EEA, including in connection with our design and potential enrollment and execution of a new clinical trial in nmDMD. We also may incur significant costs in connection with our efforts to resolve the matters set forth in the Refuse to File letter we received from the FDA with respect to our NDA for Translarna for the treatment of nmDMD, whether pursuant to continued appeal of the determination under the formal dispute resolution process or otherwise.

We anticipate that our expenses will further increase in connection with the expansion of our global infrastructure as we continue to establish an international presence and commercialize Translarna for the treatment of nmDMD, including sales and marketing, legal and regulatory, distribution and manufacturing and administrative and employee-based expenses. In addition to the foregoing, we expect to continue to incur significant costs in connection with our ongoing confirmatory Phase 3 ACT CF clinical trial and open label extension clinical trials of Translarna for the treatment of nmDMD and nmCF as well as our Phase 2 proof-of-concept studies for nmMPS I, nonsense mutation aniridia and nonsense mutation Dravet syndrome/CDKL5. We also expect to incur ongoing research and development expenses for our other product candidates, including our ongoing Phase 1 clinical study under our cancer stem cell program. In addition, we may incur substantial costs in connection with our efforts to advance our regulatory submissions, including those we have made or may make for Translarna for the treatment of nmCF, including in connection with our variation submission with the EMA, which seeks to include Translarna for the treatment of nmCF on our current marketing authorization in the EEA. We have begun seeking and intend to continue to seek marketing authorization for Translarna for the treatment of nmDMD in territories outside of the EEA and we may also seek marketing authorization for Translarna for other indications. These efforts may significantly impact the timing and extent of our commercialization expenses.

In addition, our expenses will increase if and as we:

- are required to complete any additional clinical and non-clinical trials or analyses to enable FDA review of an NDA submission by us for Translarna for the treatment of nmDMD;
- are required to take other steps to obtain or maintain our current or any further marketing authorizations we may receive for Translarna for the treatment of nmDMD, including in the EEA;
- initiate or continue the research and development of Translarna for additional indications and of our other product candidates;
- seek to discover and develop additional product candidates;
- maintain, expand and protect our intellectual property portfolio; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and commercialization efforts.

We believe that our cash flows from product sales, together with existing cash and cash equivalents, including the net proceeds from our offering of the Convertible Notes, public offerings of common stock, marketable securities and research funding that we expect to receive under our collaborations, will be sufficient to fund our operating expenses and capital expenditure requirements for at least the next twelve months. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect.

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

- the costs, timing and outcome of the annual EMA reassessment related to renewal of our marketing authorization in the EEA for Translarna for the treatment of nmDMD, including whether the EMA determines that the risk-benefit balance of Translarna supports renewal of our marketing authorization in the EEA, on the current approved label, or at all and the design of any acceptable new clinical trial in nmDMD we may be able to develop with input from the EMA, if any, including with respect to matters of scope, length, and conduct;

- the costs, timing and outcome of our efforts to resolve the matters set forth in the Refuse to File letter we received from the FDA in connection with our NDA for Translarna for the treatment of nmDMD, whether pursuant to continued appeal under the formal dispute resolution process or otherwise, and including whether we will be required to perform additional clinical and non-clinical trials or complete additional analyses at significant cost and whether such trials, if successful, may enable FDA review of a NDA submission and, ultimately, may support approval of Translarna for nmDMD in the U.S;

- the costs, timing and outcome of regulatory submissions we have made or may make for Translarna for the treatment of nmCF, including in connection with our variation submission with the EMA, which seeks to include Translarna for the treatment of nmCF on our current marketing authorization in the EEA;

- the progress and results of our confirmatory Phase 3 ACT CF trial and open label extension clinical trials of Translarna for the treatment of nmDMD and nmCF as well as our Phase 2 proof of concept studies for nmMPS I and nonsense mutation aniridia and nonsense mutation Dravet syndrome/CDKL5 and our ongoing Phase 1 clinical study under our cancer stem cell program;

- the scope, costs and timing of our commercialization activities, including product sales, marketing, legal, regulatory, distribution and manufacturing, for nmDMD and any of our other product candidates that may receive marketing authorization or any additional indications or territories in which we receive authorization to market Translarna;

- the costs, timing and outcome of regulatory review of our other product candidates and Translarna in other territories or for indications other than nmDMD and nmCF;

- the timing and scope of growth in our employee base;

- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for Translarna for additional indications and for our other product candidates;

- the number and development requirements of other product candidates that we pursue;

- revenue received from commercial sales of Translarna or any of our other product candidates;

- our ability to successfully negotiate adequate pricing and reimbursement processes on a timely basis, or at all, in the countries in which we may obtain regulatory approval, including the countries in the EEA;

- our ability to obtain additional and maintain existing reimbursed named patient and cohort EAP programs for Translarna for the treatment of nmDMD on adequate terms, or at all;

- the ability and willingness of patients and healthcare professionals to access Translarna through alternative means if pricing and reimbursement negotiations in the applicable territory do not have a positive outcome, including whether patients in Germany will continue to be able to access Translarna via a reimbursed importation pathway provided under German law and whether such pathway, if utilized, will minimize any access issues for German patients while maintaining a sustainable price;

- the costs of preparing, filing and prosecuting patent applications, maintaining, and protecting our intellectual property rights and defending against intellectual property-related claims;

- the extent to which we acquire or invest in other businesses, products and technologies; and

- our ability to establish and maintain collaborations, including our collaborations with Roche and the SMA Foundation, and our ability to obtain research funding and achieve milestones under these agreements.

With respect to our outstanding Convertible Notes, cash interest payments are payable on a semi-annual basis in arrears, which will require total funding of $4.5 million annually. Furthermore, as a result of our initial public offering in June 2013, we have incurred and expect to continue to incur additional costs associated with operating as a public company. These costs include significant legal, accounting, investor relations and other expenses that we did not incur as a private company. Additionally, we could be forced to expend significant resources in the defense of the pending securities class action lawsuits brought against us and certain of our executives, as described under Part II, Item 1. Legal Proceedings in this Quarterly Report on Form 10-Q.

We will need to generate significant revenues to achieve and sustain profitability, and we may never do so. We may need to obtain substantial additional funding in connection with our continuing operations. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs primarily through a combination of equity offerings, debt financings, collaborations, strategic alliances, grants and clinical trial support from governmental and philanthropic organizations and patient advocacy groups in the disease areas addressed by our product and product candidates and marketing, distribution or licensing arrangements. Adequate additional financing may not be available to us on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our shareholders ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us.

If we are unable to raise additional funds through equity or debt financings when needed or on attractive terms, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Off-Balance Sheet Arrangements

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

Contractual obligations

During the period ended September 30, 2016, there were no material changes to our contractual obligations and commitments outside the ordinary course of business from those disclosed under the heading “Management’s Discussion and Analysis of Financial Condition and Results of Operations-Contractual Obligations” in our Annual Report on Form 10-K for the year ended December 31, 2015.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

During the period ended September 30, 2016, there were no material changes in our market risk or how our market risk is managed, compared to those disclosed under the heading “Quantitative and Qualitative Disclosures about Market Risk” in our Annual Report on Form 10-K for the year ended December 31, 2015.

Item 4. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of September 30, 2016. The term “disclosure controls and procedures”, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company’s management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily

applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of September 30, 2016, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

No change in our internal control over financial reporting occurred during the quarter ended September 30, 2016 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II—OTHER INFORMATION

Item 1. Legal Proceedings.

In March 2016, three purported securities class action lawsuits were commenced in the United States District Court for the District of New Jersey (one each on March 3, 10, and 11), naming as defendants the Company, our Chief Executive Officer, and our Chief Financial Officer, captioned, respectively, as *Hong Wang v. PTC Therapeutics, Inc., et al.*, No. 16-cv-01224, *Kevin Kosin v. PTC Therapeutics, Inc., et al.*, No. 16-cv-01383, and *Daniel Parker v. PTC Therapeutics, Inc., et al.*, No. 16-cv-01384. The lawsuits, which have been consolidated, allege violations of Sections 10(b) and 20(a) and Rule 10b-5 of the Securities Exchange Act of 1934 in connection with allegedly false and misleading statements made by the Company about its business, operations, and prospects as it relates to the NDA for Translarna for the treatment of nmDMD that the Company submitted to the FDA in December 2015. The plaintiffs seek, among other things, compensatory damages for purchasers of the Company's common stock between May 6, 2014 and February 29, 2016, as well as attorneys' fees and costs.

Item 1A. Risk Factors

The following risk factors and other information included in this Quarterly Report on Form 10-Q should be carefully considered. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 3 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 and Need for Additional Capital

We have incurred significant losses since our inception. We may never generate profits from operations or maintain profitability and expect to continue to incur significant operating losses and expenses for at least the next several years in connection with our efforts, among other things, to:

- ***maintain our marketing authorization for Translarna™ (ataluren) for the treatment of nonsense mutation Duchenne muscular dystrophy, or nmDMD, in the European Economic Area, or EEA, which if renewal is granted, we expect will require us to conduct an agreed upon new clinical trial in Translarna for nmDMD;***
- ***resolve the matters set forth in the Refuse to File letter we received from the U.S. Food and Drug Administration, or FDA, in connection with our New Drug Application, or NDA, for Translarna for the treatment of nmDMD, in particular pursuant to continued appeal under the formal dispute resolution process;***
- ***continue expansion of our global operations and execution of our commercial strategy for Translarna in the EEA and other territories; and***
- ***obtain broader and additional regulatory approvals for Translarna and advance the development of our product pipeline.***

Since inception, we have incurred significant operating losses. As of September 30, 2016, we had an accumulated deficit of $708.3 million. We have historically financed our operations primarily through the issuance and sale of our common stock in public offerings, the private placements of our preferred stock, collaborations, bank debt, convertible debt financings, and grants and clinical trial support from governmental and philanthropic organizations and patient advocacy groups in the disease areas addressed by our product and product candidates. We expect to continue to incur significant expenses and operating losses for at least the next several years. The net losses we incur may fluctuate significantly from quarter to quarter.

In October 2015, we announced the initial results of ACT DMD, our Phase 3 trial for Translarna™ (ataluren) for the treatment of nmDMD, including that the primary efficacy endpoint in the intent to treat, or ITT, population did not achieve statistical significance. Please review the risk factor under "Risks Related to the Development and Commercialization of our Product and

our Product Candidates" titled, "*ACT DMD, our Phase 3 trial for Translarna for the treatment of nmDMD, did not meet its primary efficacy endpoint, and we received a Refuse to File letter from the FDA for our NDA submitted with data from this trial and the FDA recently denied our first appeal of the Refuse to File letter, the EMA is questioning the positive risk-benefit balance of Translarna for the treatment of nmDMD based on data from this trial and the CHMP has requested that we submit a proposal for a new clinical trial in nmDMD, and there is substantial risk that other regulators will not agree with our interpretation of the results of ACT DMD and the totality of clinical data from our trials in Translarna for the treatment of nmDMD, which would have a material adverse effect on our business, financial performance and results of operations.*" for a review of recent developments that have had, and may continue to have, a material adverse effect on our ability to obtain or maintain marketing authorizations necessary to commercialize Translarna for the treatment of nmDMD in the United States, Europe and other territories, including: our receipt of a Refuse to File letter from the FDA with respect to our NDA for Translarna for the treatment of nmDMD; the FDA's recent denial of our appeal of the Refuse to File determination; the EMA's questioning of the positive risk-benefit balance of Translarna for the treatment of nmDMD, which is required in order for the EMA's CHMP to issue a positive opinion in favor of annual renewal of our marketing authorization to the European Commission; and the likelihood that if the CHMP issues a positive opinion in favor of the renewal of Translarna's marketing authorization, such renewal, and any subsequent annual renewals, will be coupled with an obligation to conduct an agreed upon new clinical trial of Translarna for the treatment of nmDMD.

Our ability to generate revenue is almost entirely dependent upon our ability to maintain our marketing authorization for Translarna in the EEA for the treatment of nmDMD in ambulatory patients aged five years and older. In order to continue commercial sales and our commercial launch of Translarna we must maintain our marketing authorization. The marketing authorization, initially granted in August 2014, is subject to annual review and renewal by the European Commission following reassessment by the EMA of the risk-benefit balance of the authorization, which we refer to as the annual EMA reassessment, as well as our satisfaction of other conditions and obligations placed upon the marketing authorization. As of the date of this filing, the EMA's CHMP has not issued an opinion with respect to our most recent request for renewal of our marketing authorization.

We have submitted our responses to requests for supplemental information, or RSI, received from the CHMP in October 2016. The RSI, which included a request classified as a major objection, were related to the efficacy and overall risk-benefit profile of Translarna as well as the design and conduct of an additional clinical trial that would provide comprehensive clinical data on these matters. Generally speaking, a failure to adequately address a major objection would preclude a recommendation for renewal of a marketing authorization. The extended duration of this renewal request cycle and some of the recent feedback we have received as part of the annual EMA reassessment process have introduced a greater degree of uncertainty as to whether we will receive a positive opinion from the CHMP. While we expect that the CHMP will issue an opinion with respect to our renewal request by the end of 2016, there is substantial risk that the CHMP will not determine that the risk-benefit balance of Translarna supports renewal of our marketing authorization in the EEA, on the current approved label, or at all. While the EMA has not formally declined our type II variation request for full approval of our marketing authorization, we believe that it is unlikely that the EMA will recommend in favor of this request.

In addition, we continue to believe that if the CHMP issues a positive opinion in favor of the renewal of Translarna's marketing authorization, such renewal, and any subsequent annual renewals, will be coupled with an obligation to conduct an agreed upon new clinical trial of Translarna for the treatment of nmDMD. Designing, enrolling, conducting and completing a clinical trial is a time-consuming, expensive and uncertain process that takes years to complete, and we expect that in the event that we proceed with such trial, we would incur material ongoing costs related to the development of such a trial in the short-term, as well as the implementation of the trial in the longer term. Any such trial may require us to enroll patients in countries where Translarna is currently available on a reimbursed basis, which could impact growth in our net product sales. However, the CHMP may issue a negative opinion against renewal of the marketing authorization on the basis that, in the committee's view, the balance of risks and benefits of using Translarna for the treatment of nmDMD has changed materially. In such an event the European Commission could, at the EMA's recommendation, vary, suspend, withdraw or refuse to renew the marketing authorization for Translarna.

Even if the CHMP determines to issue a positive opinion, the EMA may impose other new conditions to our marketing authorization (in addition to the potential clinical trial described above) and may make other recommendations, including new label restrictions. In the event that we do secure annual renewal of the marketing authorization, the EMA could nevertheless later determine that we have not complied, or are unable to comply, with any conditions that have been or may be placed on the marketing authorization, which again could result in the withdrawal of our marketing authorization or other outcome that would have a materially adverse effect on our business.

We expect to incur significant costs in connection with our efforts to maintain our marketing authorization in the EEA. If our marketing authorization in the EEA is not renewed, or our product label is materially restricted, we would lose all, or a

significant portion of, our ability to generate revenue from product sales, whether pursuant to a commercial or an early access program, or EAP, and throughout all territories.

For additional information regarding the risks related to renewal of our marketing authorization in the EEA, see the risk factor under "Risks Related to Regulatory Approval of our Product and our Product Candidates" titled, "*Our marketing authorization in the EEA requires annual renewal by the European Commission, which, as of the date of this filing, has not been granted, and there is substantial risk that the EMA will not determine that the risk-benefit balance of Translarna supports renewal of our marketing authorization, on the current label, or at all, and, even if the European Commission grants renewal of our marketing authorization, such renewal will likely be conditioned upon the results of a not yet designed trial for Translarna for the treatment of nmDMD, which will likely result in significant expense and uncertainty for us. If we are not able to obtain renewal of our marketing authorization, we will not be able to continue to commercialize Translarna for nmDMD and our ability to generate revenue will be materially impaired.*"

We recently initiated a formal dispute resolution with the FDA, seeking to reverse the FDA's Refuse to File decision. In October 2016, the FDA denied our first appeal of the Refuse to File letter. Although we intend to continue our appeal of the Refuse to File determination to progressively higher levels of FDA management under the ongoing formal dispute resolution process, we expect that our efforts to resolve the matters set forth in the Refuse to File letter, whether pursuant to this appeal or otherwise, will be time-consuming and may be expensive and there is significant risk that we will not be successful in obtaining FDA review of our NDA for Translarna for nmDMD in a timely fashion, if ever. Even if we are successful in reversing the Refuse to File decision, there is significant risk that we will be unable to obtain FDA approval of Translarna for nmDMD and we may be required to perform additional clinical and non-clinical trials or analyses at significant cost which, if successful, may enable FDA review of an NDA submission by us and, ultimately, may support approval of Translarna for nmDMD in the U.S. An inability to obtain new marketing authorizations for Translarna for nmDMD, including in the United States would have a material adverse effect on our ability to generate revenue from the sales of Translarna for the treatment of nmDMD. For additional information, see the risk factor under "Risks Related to Regulatory Approval of our Product and our Product Candidates" titled, "*The FDA denied our first appeal of the Refuse to File letter we received from the agency regarding our NDA for Translarna for the treatment of nmDMD, there is substantial risk that we will not be successful in further appeals of the Refuse to File letter to progressively higher levels of the FDA, and by determining to continue to pursue our appeal under the formal dispute resolution process with the FDA, we have postponed other available strategic pathways which may have proven to be more effective. If there are delays in obtaining regulatory approval in the United States, we will not be able to commercialize Translarna for nmDMD in that territory and our ability to generate revenue will be materially impaired.*"

We anticipate that our expenses will further increase in connection with the expansion of our global infrastructure as we continue to establish an international presence and commercialize Translarna for the treatment of nmDMD, including sales and marketing, legal and regulatory, distribution and manufacturing and administrative and employee-based expenses. In addition, the clinical and regulatory developments noted in this risk factor may exacerbate the risks related to our commercialization efforts set forth under the heading "Risks Related to the Development and Commercialization of our Product and our Product Candidates," which could increase the costs associated with our commercial activities. For additional information, see also, the risk factor under the heading "Risks Related to the Regulation of our Product and our Product Candidates" titled "*Our initial commercial launch of Translarna has begun in, and is expected to continue to take place in, countries that tend to impose strict price controls, which may adversely affect our revenues, if any. Failure to obtain and maintain acceptable pricing and reimbursement terms for Translarna in the European Economic Area and other jurisdictions would prevent us from marketing our products in such regions.*"

In addition to the foregoing, we expect to continue to incur significant costs in connection with our ongoing confirmatory Phase 3 ACT CF clinical trial and open label extension clinical trials of Translarna for the treatment of nmDMD and nmCF as well as our Phase 2 proof-of-concept studies for nmMPS I, nonsense mutation aniridia and nonsense mutation Dravet syndrome/CDKL5. We also expect to incur ongoing research and development expenses for our other product candidates, including our ongoing Phase 1 clinical study under our cancer stem cell program. In addition, we may incur substantial costs in connection with our efforts to advance our regulatory submissions, including those we have made or may make for Translarna for the treatment of nmCF, including in connection with our variation submission with the EMA, which seeks to include Translarna for the treatment of nmCF on our current marketing authorization in the EEA. We have begun seeking and intend to continue to seek marketing authorization for Translarna for the treatment of nmDMD in territories outside of the EEA and we may also seek marketing authorization for Translarna for other indications. These efforts may significantly impact the timing and extent of our commercialization expenses. With respect to our outstanding 3.00% convertible senior notes due August 15, 2022, or the Convertible Notes, cash interest payments are payable on a semi-annual basis in arrears, which will require total funding of $4.5 million annually.

In addition, our expenses will increase if and as we:

- are required to complete any additional clinical and non-clinical trials or analyses to enable FDA review of an NDA submission by us for Translarna for the treatment of nmDMD;
- are required to take other steps to obtain or maintain our current or any further marketing authorizations we may receive for Translarna for the treatment of nmDMD, including in the EEA;
- initiate or continue the research and development of Translarna for additional indications and of our other product candidates;
- seek to discover and develop additional product candidates;
- maintain, expand and protect our intellectual property portfolio; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and commercialization efforts.

We also could be forced to expend significant resources in the defense of the pending securities class action lawsuits brought against us and certain of our executives, as described under Part II, Item 1. Legal Proceedings in this Form 10-Q.

Our ability to generate profits from operations and become and remain profitable depends on our ability to successfully develop and commercialize drugs that generate significant revenue. This will require us to be successful in a range of challenging activities, including:

- completing our confirmatory Phase 3 ACT CF clinical trial of Translarna;
- maintaining the marketing authorization of Translarna for the treatment of nmDMD in the EEA and satisfying all related conditions and ongoing requirements, including successfully developing and conducting an agreed upon new clinical trial designed with scientific advice from the EMA;
- successfully preparing and advancing regulatory submissions for Translarna for the treatment of nmCF, including advancement of our current variation submission with the EMA, which seeks to include Translarna for the treatment of nmCF on our current marketing authorization in the EEA;
- resolving the matters set forth in the Refuse to File letter we received from the FDA in connection with our NDA for Translarna for the treatment of nmDMD in a timely manner or at all, whether pursuant to continued appeal under the formal dispute resolution process, or otherwise and including, if required, performing additional clinical and non-clinical trials or analyses at significant cost which, if successful, may enable FDA review of an NDA submission by us and, ultimately, may support approval of Translarna for nmDMD in the U.S.;
- expanding the territories in which we are approved to market Translarna for the treatment of nmDMD;
- initiating clinical studies of Translarna for the treatment of additional indications, including nmMPS I, nonsense mutation aniridia, and nonsense mutation Dravet syndrome/CDKL5 and successfully advancing our other programs and collaborations, including our cancer stem cell and SMA programs;
- establishing a global commercial infrastructure, including the sales, marketing and distribution capabilities to effectively market and sell Translarna in Europe, the United States, and other parts of the world;
- implementing marketing and distribution relationships with third parties in territories where we do not pursue direct commercialization;
- negotiating and securing adequate pricing and reimbursement terms for Translarna on a timely basis, or at all, in the countries in which we have obtained, and may obtain, regulatory approval;
- negotiating and securing adequate reimbursement from other third-party payors for Translarna;
- launching commercial sales of Translarna for the treatment of nmDMD in accordance with our estimated timeline;

- identifying patients eligible for treatment with Translarna;
- obtaining approval to market Translarna for the treatment of other indications;
- expanding the approved product label of Translarna for the treatment of nmDMD;
- protecting our rights to our intellectual property portfolio related to Translarna; and
- contracting for the manufacture and distribution of commercial quantities of Translarna.

We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to generate profits from operations. Even if we do generate profits from operations, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to generate profits from operations and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment in our company.

We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

As noted in the prior risk factor, we expect to incur significant expenses related to our clinical, regulatory, commercial, legal, research and development, and other business efforts. We believe that our cash flows from product sales, together with existing cash and cash equivalents, including the net proceeds from our Convertible Note offering, public offerings of common stock, marketable securities and research funding that we expect to receive under our collaborations, will be sufficient to fund our operating expenses and capital expenditure requirements for at least the next twelve months. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect.

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

- the costs, timing and outcome of the annual EMA reassessment related to renewal of our marketing authorization in the EEA for Translarna for the treatment of nmDMD, including whether the EMA determines that the risk-benefit balance of Translarna supports renewal of our marketing authorization in the EEA, on the current approved label, or at all and the design of any agreed upon new clinical trial in nmDMD we may be required to conduct, if any, including with respect to matters of scope, length, and conduct;
- the costs, timing and outcome of our efforts to resolve the matters set forth in the Refuse to File letter we received from the FDA in connection with our NDA for Translarna for the treatment of nmDMD, whether pursuant to continued appeal of the Refuse to File pursuant to the ongoing formal dispute resolution process or otherwise, and including whether we will be required to perform additional clinical and non-clinical trials or complete additional analyses at significant cost and whether such trials, if successful, may enable FDA review of a NDA submission and, ultimately, may support approval of Translarna for nmDMD in the U.S.;
- the costs, timing and outcome of regulatory submissions we have made or may make for Translarna for the treatment of nmCF, including in connection with our variation submission with the EMA, which seeks to include Translarna for the treatment of nmCF on our current marketing authorization in the EEA;
- the progress and results of our confirmatory Phase 3 ACT CF trial and open label extension clinical trials of Translarna for the treatment of nmDMD and nmCF as well as our Phase 2 proof-of-concept studies for nmMPS I and nonsense mutation aniridia and nonsense mutation Dravet syndrome/CDKL5 and our ongoing Phase 1 clinical study under our cancer stem cell program;
- the scope, costs and timing of our commercialization activities, including product sales, marketing, legal, regulatory, distribution and manufacturing, for nmDMD and any of our other product candidates that may receive marketing authorization or any additional indications or territories in which we receive authorization to market Translarna;
- the costs, timing and outcome of regulatory review of our other product candidates and Translarna in other territories or for indications other than nmDMD and nmCF;
- the timing and scope of growth in our employee base;

- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for Translarna for additional indications and for our other product candidates;
- the number and development requirements of other product candidates that we pursue;
- revenue received from commercial sales of Translarna or any of our other product candidates;
- our ability to successfully negotiate adequate pricing and reimbursement processes on a timely basis, or at all, in the countries in which we may obtain regulatory approval, including the countries in the EEA;
- our ability to obtain additional and maintain existing reimbursed named patient and cohort EAP programs for Translarna for the treatment of nmDMD on adequate terms, or at all;
- the ability and willingness of patients and healthcare professionals to access Translarna through alternative means if pricing and reimbursement negotiations in the applicable territory do not have a positive outcome, including whether patients in Germany will continue to be able to access Translarna via a reimbursed importation pathway provided under German law and whether such pathway, if utilized, will minimize any access issues for German patients while maintaining a sustainable price;
- the costs of preparing, filing and prosecuting patent applications, maintaining, and protecting our intellectual property rights and defending against intellectual property-related claims;
- the extent to which we acquire or invest in other businesses, products and technologies; and
- our ability to establish and maintain collaborations, including our collaborations with Roche and the SMA Foundation, and our ability to obtain research funding and achieve milestones under these agreements.

Conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales for certain product candidates or indications. In addition, our product candidates, if approved, may not achieve commercial success, including Translarna for the treatment of nmDMD.

We are continuing to engage in significant commercialization efforts for Translarna for nmDMD. We commenced our commercial launch of Translarna in Germany in December 2014 and we expect to commercially launch in other key countries in the EEA in 2016 and in future years, subject to completion of pricing and reimbursement negotiations. In the third quarter of 2014, we began to recognize revenue for payments received under reimbursed EAP programs for Translarna for nmDMD patients in selected countries. In order to continue commercial sales and our commercial launch of Translarna we must maintain our marketing authorization in the EEA. We expect that any commercial revenue generated in the next several years will be derived exclusively from sales of Translarna for the treatment of nmDMD and other indications, if any, that may receive marketing authorization and that commercial sales will generally be limited to countries in the EEA and other territories in which we have obtained marketing authorization and reimbursement approval or are permitted to initiate treatment under reimbursed EAP programs or pursuant to other procedures. Other commercial revenue, if any, would be derived from sales of products that we are not planning to have commercially available for several years, if at all. If our marketing authorization in the EEA is not renewed, or our product label is materially restricted, we would lose all, or a significant portion of, our ability to generate revenue from product sales, whether pursuant to a commercial or an EAP program and throughout all territories.

Accordingly, we will need to continue to rely on additional financing in connection with our continuing operations and to achieve our business objectives. In addition, we may seek additional capital due to favorable market conditions or based on strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. Additional financing may not be available to us on acceptable terms or at all. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or our commercialization efforts.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings; debt financings; collaborations; strategic alliances; grants and clinical trial support from

governmental and philanthropic organizations and patient advocacy groups in the disease areas addressed by our product candidates; and marketing, distribution or licensing arrangements.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, our shareholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates; or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our limited operating history may make it difficult for our stockholders to evaluate the success of our business to date and to assess our future viability.

In the third quarter of 2014 we began to recognize revenue for payments received under reimbursed EAP programs for Translarna for nmDMD patients in selected countries, and we commenced our commercial launch of Translarna in Germany in December 2014. Prior to such time, our operations were limited to organizing and staffing our company, developing and securing our technology, raising capital, undertaking preclinical studies and clinical trials of our product candidates, and preparing for the commercial launch of Translarna for nmDMD in Europe. We are in the process of transitioning from a company with a research and development focus to a company capable of supporting global commercial activities. We may not be successful in such a transition. We have not proven our ability to successfully obtain marketing authorizations to sell our product or product candidates, other than with respect to the marketing authorization granted by the European Commission in August 2014 for Translarna for the treatment of nmDMD, which is subject to annual review and renewal following reassessment of the risk-benefit balance of the authorization by the EMA and satisfaction of any conditions that may be imposed by the EMA, and the marketing authorizations granted in Israel and South Korea (which are largely contingent upon continued EMA approval). In addition, we have not yet demonstrated our ability to complete development of product candidates, manufacture a commercial scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for a successful full scale product commercialization. Consequently, any predictions our stockholders make about our future success or viability may not be as accurate as they could be if we had a longer operating history. In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors.

Our ability to use our net operating losses and certain other tax attributes may be subject to annual limitations under federal and state tax law that could materially affect our ability to utilize such losses and attributes.

If a corporation undergoes an "ownership change" within the meaning of Section 382 of the Internal Revenue Code, or Section 382, the corporation's ability to utilize any net operating losses, or NOLs, and certain tax credits and other attributes generated before such an ownership change, is limited. We believe that we have in the past experienced ownership changes within the meaning of Section 382 that have resulted in limitations under Section 382 (and similar state provisions) on the use of our NOLs and other tax attributes.

Future changes in ownership could result in additional ownership changes within the meaning of Section 382 that could further limit our ability to utilize our NOLs and certain other tax attributes.

Changes in our effective income tax rates could adversely affect our results of operations.

We are subject to income taxes in the Unites States and various foreign jurisdictions. Taxes will be incurred as income is earned among these different jurisdictions. Various factors may have favorable or unfavorable effects on our effective income tax rate. These factors include, but are not limited to, interpretations of existing tax laws, changes in tax laws and rates, the accounting for stock options and other share-based compensation, changes in accounting standards, future levels of research and development spending, changes in the mix and level of pre-tax earnings by taxing jurisdiction, the outcome of examinations by the U.S. Internal Revenue Service and other jurisdictions, the accuracy of our estimates for unrecognized tax benefits, the realization of deferred tax assets, or by changes to our ownership or capital structure. The impact on our income tax provision resulting from the above-mentioned factors and others may be significant and could adversely affect our results of operations.

Risks Related to the Development and Commercialization of our Product and our Product Candidates

ACT DMD, our Phase 3 trial for Translarna for the treatment of nmDMD, did not meet its primary efficacy endpoint, and we received a Refuse to File letter from the FDA for our NDA submitted with data from this trial and the FDA recently denied our first appeal of the Refuse to File letter, the EMA is questioning the positive risk-benefit balance of Translarna for the treatment of nmDMD based on data from this trial and the CHMP has requested that we submit a proposal for a new clinical trial in nmDMD, and there is substantial risk that other regulators will not agree with our interpretation of the results of ACT DMD and the totality of clinical data from our trials in Translarna for the treatment of nmDMD, which would have a material adverse effect on our business, financial performance and results of operations.

In October 2015, we announced the initial results of ACT DMD, including that the primary efficacy endpoint in the intent to treat, or ITT, population did not achieve statistical significance. On the basis of our position that the totality of clinical data from ACT DMD and our prior Phase 2b trial support the clinical benefit of Translarna for the treatment of nmDMD, we submitted our analyses of the ACT DMD data and meta-analysis of the combined ACT DMD and Phase 2b subgroup data to the FDA, as part of our NDA. On February 22, 2016, we received a Refuse to File letter from the FDA stating that, in the view of the FDA, both our Phase 2b and Phase 3 ACT DMD trials were negative and do not provide substantial evidence of effectiveness. Additionally, the FDA stated that we had proposed a post-hoc adjustment of ACT DMD that eliminates data from a majority of enrolled patients. In addition, the FDA noted that our NDA does not contain adequate information regarding the abuse potential of Translarna.

In October 2016, the FDA denied our first appeal of the Refuse to File letter. Although we intend to continue our appeal of the Refuse to File determination to progressively higher levels of FDA management, there is substantial risk that, notwithstanding any dialogue we have had or any further dialogue we may be able to initiate with the agency, including pursuant to continued appeal under the formal dispute resolution process or otherwise, the FDA will continue to disagree with our interpretation of the results of ACT DMD and the totality of clinical data from our trials. Even if we are successful in reversing the Refuse to File decision, there is significant risk that we will be unable to obtain FDA approval of Translarna for nmDMD and we may be required to perform additional clinical and non-clinical trials or complete additional analyses at significant cost, which, if we are successful in enrolling, funding, and completing, may enable FDA review of an NDA submission. Any such requirement for additional trials would most likely result in our inability to sell Translarna in the United States for a significant period of time, if ever, which would have a material adverse effect on our ability to generate revenue from the sales of Translarna for the treatment of nmDMD. Due to these uncertainties, we are unable to estimate the timing or potential for a launch of Translarna for the treatment of nmDMD in the United States.

We also submitted our analyses of the ACT DMD data and meta-analyses of the combined ACT DMD and Phase 2b subgroup data to the EMA to support continuation of our marketing authorization in the EEA, which is subject to annual review and renewal by the European Commission following reassessment by the EMA of the risk-benefit balance of the authorization. Our ability to generate revenue is almost entirely dependent upon our ability to maintain our marketing authorization for Translarna in the EEA for the treatment of nmDMD in ambulatory patients aged five years and older. As of the date of this filing, the EMA's CHMP has not issued an opinion with respect to our most recent request for renewal of our marketing authorization.

We have submitted our responses to the CHMP's most recent requests for supplemental information, or RSI, received by us in October 2016 in connection with our marketing authorization renewal submission. The RSI, which included a request classified as a major objection, were related to the efficacy and overall risk-benefit profile of Translarna as well as the design and conduct of a potential new clinical trial that would be able to demonstrate in a nmDMD patient population a robust and clinically meaningful effect of Translarna which would confirm the positive risk-benefit ratio of Translarna and address outstanding uncertainties about efficacy. Generally speaking, a failure to adequately address a major objection would preclude a recommendation for renewal of a marketing authorization. The RSI also includes requests categorized as other concerns, which do not rise to the level of a major objection, and are generally associated with long-term risk and labeling matters as well as the primary pharmacology of Translarna.

The extended duration of this renewal request cycle and some of the recent feedback we have received as part of the annual EMA reassessment process have introduced a greater degree of uncertainty as to whether we will receive a positive opinion from the CHMP. While we expect the CHMP will issue an opinion with respect to our renewal request by the end of 2016, there is substantial risk that the EMA will not determine that the risk-benefit balance of Translarna supports renewal of our marketing authorization in the EEA, on the current approved label, or at all. If, the CHMP issues a negative opinion with respect to renewal of the marketing authorization, the European Commission could, at the EMA's recommendation, withdraw or refuse to renew the marketing authorization for Translarna

In addition, we continue to believe that if the EMA's CHMP issues a positive opinion in favor of the renewal of Translarna's marketing authorization, such renewal, and any subsequent annual renewals, will be coupled with an obligation to conduct an agreed upon new clinical trial of Translarna for the treatment of nmDMD. Designing, enrolling, conducting and completing a clinical trial is a time-consuming, expensive and uncertain process that takes years to complete, and we expect that we will incur material ongoing costs related to the development and implementation of any such trial. Any new trial could also require us to enroll patients in countries where Translarna is currently available on a reimbursed basis, which could impact growth in our net product sales.

Even if the CHMP determines to issue a positive opinion, the EMA may impose other new conditions to our marketing authorization (in addition to the potential clinical trial described above) and may make other recommendations, including new label restrictions. In the event that we do secure annual renewal of the marketing authorization, the EMA could nevertheless later determine that we have not complied, or are unable to comply, with any conditions that have been or may be placed on the marketing authorization, which again could result in the withdrawal of our marketing authorization or other outcome that would have a materially adverse effect on our business. If our marketing authorization in the EEA is not renewed, or our product label is materially restricted, we would lose all, or a significant portion of, our ability to generate revenue from product sales, whether pursuant to a commercial or an early access program, or EAP, and throughout all territories.

There is substantial risk that other regulators where we have not yet sought marketing authorization will not agree with our interpretation of the results of ACT DMD and the totality of clinical data from our trials in Translarna for the treatment of nmDMD, which would have a material adverse effect on our ability to generate revenue from the sales of Translarna for the treatment of nmDMD in those applicable territories. In addition, we may not be able to maintain or obtain marketing authorizations in areas where such authorizations are contingent upon decisions of the EMA with respect to our marketing authorization in the EEA.

An inability to generate revenue from sales of Translarna for the treatment of nmDMD would have a material adverse effect on our business, financial performance and results of operations.

For additional information, see "Risk Factors Risks Related to Regulatory Approval of our Product and our Product Candidates" below.

We depend heavily on the success of our lead product, Translarna, which we are developing for nmDMD, nmCF, and other indications. All of our other product candidates, including those under our collaboration with Roche and the SMA Foundation, are still in early clinical or preclinical development. If we are unable to execute our commercial strategy for Translarna for the treatment of nmDMD in the European Economic Area, fail to receive regulatory approval in the United States and other territories, fail to obtain renewal of, or satisfy the conditions of our marketing authorization in the European Economic Area, or if we experience significant delays in accomplishing such goals, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources in the development of Translarna for nmDMD and nmCF. Additionally, we are pursuing proof of concept studies for Translarna in additional indications: nmMPS I, nonsense mutation aniridia, and nonsense mutation Dravet syndrome/CDKL5. Our ability to generate product revenues will depend heavily on the successful development and commercialization of Translarna.

In August 2014, Translarna was granted marketing authorization in the EEA for the treatment of nmDMD in ambulatory patients aged five years and older, which is subject to annual EMA reassessment and was further conditioned on our submission of the final report, including additional efficacy and safety data, from ACT DMD, which we submitted to the EMA in January 2016. In February 2016, we submitted a marketing authorization renewal request with the EMA. As of the date of this filing, the EMA's CHMP has not issued an opinion with respect to our most recent request for renewal of our marketing authorization in the EEA and the extended duration of this renewal request cycle and some of the recent feedback we have received as part of the annual EMA reassessment process have introduced a greater degree of uncertainty as to whether we will receive a positive opinion from the CHMP. Our ability to generate revenue is almost entirely dependent upon our ability to maintain our marketing authorization for Translarna in the EEA for the treatment of nmDMD in ambulatory patients aged five years and older. In order to continue commercial sales and our commercial launch of Translarna we must maintain our marketing authorization. Translarna is still under investigation for the treatment of nmDMD in the United States and has not been approved by the FDA.

Please review the foregoing risk factor titled, "*ACT DMD, our Phase 3 trial for Translarna for the treatment of nmDMD, did not meet its primary efficacy endpoint, and we received a Refuse to File letter from the FDA for our NDA submitted with data from this trial and the FDA recently denied our first appeal of the Refuse to File letter, the EMA is questioning the positive risk-*

benefit balance of Translarna for the treatment of nmDMD based on data from this trial and the CHMP has requested that we submit a proposal for a new clinical trial in nmDMD, and there is substantial risk that other regulators will not agree with our interpretation of the results of ACT DMD and the totality of clinical data from our trials in Translarna for the treatment of nmDMD, which would have a material adverse effect on our business, financial performance and results of operations" for a review of recent developments that have had, and may continue to have, a material adverse effect on our ability to commercialize Translarna for the treatment of nmDMD, including: our receipt of a Refuse to File letter from the FDA with respect to our NDA for Translarna for the treatment of nmDMD; the FDA's recent denial of our appeal of the Refuse to File determination; the EMA's questioning of the positive risk-benefit balance of Translarna for the treatment of nmDMD, which is required in order for the CHMP to issue a positive opinion in favor of annual renewal of our marketing authorization to the European Commission; and the likelihood that if the CHMP issues a positive opinion in favor of the renewal of Translarna's marketing authorization, such renewal, and any subsequent annual renewals, will be coupled with an obligation to conduct an agreed upon new clinical trial of Translarna for the treatment of nmDMD.

If we do not successfully renew and maintain our marketing authorization and commercialize Translarna in the EEA, or receive regulatory approval in the United States for Translarna for the treatment of nmDMD and subsequently successfully commercialize Translarna in the United States, our ability to generate additional revenue will be jeopardized and, consequently, our business will be materially harmed.

The success of Translarna will depend on a number of additional factors, including the following:

- whether the EMA and the European Commission determine that the risk-benefit balance of Translarna for the treatment of nmDMD supports renewal of our marketing authorization in the EEA, on the current approved label, or at all, and the timelines within which such determinations are made;
- the design of any clinical trial we develop with scientific advice from the EMA and its advisors, including, but not limited to matters of size, duration and scope;
- whether, and within what timeframe, we are able to resolve the matters set forth in the Refuse to File letter we received from the FDA in connection with our NDA for Translarna for the treatment of nmDMD, pursuant to continued appeal under the formal dispute resolution process, or otherwise, and including whether we will be required to perform additional clinical and non-clinical trials or analyses, the costs of such trials or analyses, and whether such trials or analyses, if successful, may enable FDA review of a NDA submission and, ultimately, may support approval of Translarna for nmDMD in the U.S.;
- successful completion of our confirmatory Phase 3 ACT CF clinical trial of Translarna;
- our ability to successfully prepare and advance regulatory submissions for Translarna for the treatment of nmCF, including with respect to our variation submission with the EMA, which seeks to include Translarna for the treatment of nmCF on our current marketing authorization in the EEA;
- the successful advancement of Translarna in additional indications, in particular, nmMPS I, nonsense mutation aniridia, and nonsense mutation Dravet syndrome/CDKL5;
- the establishment of an expanded international commercial infrastructure capable of supporting product sales, marketing, and distribution of Translarna;
- implementing marketing and distribution relationships with third parties in territories where we do not pursue direct commercialization;
- the continued maintenance of, and satisfaction of the conditions and ongoing requirements under, the marketing authorization of Translarna for the treatment of nmDMD in the EEA;
- our ability to obtain additional and maintain existing reimbursed named patient and cohort EAP programs for Translarna for the treatment of nmDMD on adequate terms;
- whether and when we obtain marketing authorization of Translarna in additional territories and for additional or expanded indications;

- successful negotiation of adequate pricing and reimbursement terms for Translarna on a timely basis, or at all, in the countries which require such negotiation and in which we obtain regulatory approval;
- the ability and willingness of patients and healthcare professionals to access Translarna through alternative means if pricing and reimbursement negotiations in the applicable territory do not have a positive outcome, including whether patients in Germany will continue to be able to access Translarna via a reimbursed importation pathway provided under German law and whether such pathway, if utilized, will minimize any access issues for German patients while maintaining a sustainable price;
- the timing and scope of commercial launches of Translarna in nmDMD;
- our ability to establish and maintain commercial manufacturing arrangements with third party manufacturers;
- the ability of our third-party manufacturers to successfully produce commercial and clinical supplies of Translarna on a timely basis sufficient to meet the needs of our commercial and clinical activities;
- successful identification of eligible patients;
- acceptance of Translarna in nmDMD by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- a continued acceptable safety profile of Translarna;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity; and
- protecting our rights in our intellectual property portfolio.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to continue to commercialize Translarna, which would materially harm our business.

The marketing authorization granted by the European Commission for Translarna for the treatment of nmDMD is subject to the satisfaction of specific conditions and is limited to ambulatory patients aged five years and older located in the European Economic Area, which significantly limits an already small treatable patient population, reduces our commercial opportunities, is subject to annual reassessment of the risk-benefit balance by the EMA and other requirements, and may be varied, suspended or withdrawn by the European Commission if we fail to satisfy those requirements.

We have obtained orphan drug designations from the EMA and from the FDA for Translarna for the treatment of nmDMD because the number of patients who could benefit from treatment with Translarna is small. The marketing label approved by the European Commission further limits the currently treatable patient population to ambulatory nmDMD patients aged five years and older who have been identified through genetic testing. Prevalence estimates for rare diseases are typically provided in ranges due to the uncertainties associated with the methodologies used to derive estimates such as epidemiology assumptions. It can take many years of experience in rare disease market places before prevalence becomes well characterized. We are launching the first therapy specifically aimed at DMD patients and in particular DMD patients with a nonsense mutation. Our experience to date suggests that there may be up to 7,000 nmDMD patients globally and that approximately 40% of such patients are qualified for treatment under our current product label in the EEA. Country specific epidemiology will continue to be refined and characterized over the coming years and we have determined that we are not able to provide or confirm prior prevalence estimates on a country or regional basis at this time. Our estimates of both the number of people who have DMD caused by a nonsense mutation, as well as the subset of people with nmDMD who are ambulatory and at least five years old, are based on our beliefs and estimates derived from a variety of sources and may prove to be incorrect. Prevalence estimates vary given some degree of variation in the incidence of live male births, the incidence of DMD, the incidence nonsense mutations and other factors. Information concerning the eligible patient population is generally limited to certain geographies and may not employ definitive measures capable of establishing with precision the actual number of nmDMD patients in such geography. If the market opportunities for Translarna for the treatment of nmDMD are smaller than we believe they are, our business and anticipated revenues will be negatively impacted. Although we intend to seek to expand the approved product label of Translarna for the treatment of nmDMD in the future, the timing of, and our ability to generate, the necessary data or results required to obtain expanded regulatory approval is currently uncertain. Given the small number of patients who have nmDMD, and the smaller number of patients who meet the criteria for treatment under our current marketing authorization, our

commercial opportunity is limited. It is critical to the commercial success of Translarna for nmDMD that we successfully identify and treat these patients.

Our ability to generate revenue is almost entirely dependent upon our ability to maintain our marketing authorization for Translarna in the EEA for the treatment of nmDMD in ambulatory patients aged five years and older. In order to continue commercial sales and our commercial launch of Translarna we must maintain our marketing authorization. The marketing authorization, initially granted in August 2014, is subject to annual review and renewal by the European Commission following reassessment by the EMA of the risk-benefit balance of the authorization, which we refer to as the annual EMA reassessment, as well as our satisfaction of other conditions and obligations placed upon the marketing authorization. As of the date of this filing, the EMA's CHMP has not issued an opinion with respect to our most recent request for renewal of our marketing authorization.

There is substantial risk that the EMA will not determine that the risk-benefit balance of Translarna supports renewal of our marketing authorization in the EEA, on the current approved label, or at all. In addition, we believe that if the EMA's CHMP does determine to issue a positive opinion in favor of renewing our annual marketing authorization, such renewal, and any subsequent annual renewals, will be coupled with an obligation to conduct an agreed upon new clinical trial of Translarna for the treatment of nmDMD, designed with the scientific advice of the EMA. The CHMP has noted that this trial must be deemed feasible in the post-authorization setting. Enrolling a new clinical trial to evaluate Translarna for the treatment of nmDMD may further reduce the number of patients available for reimbursed treatment. If the EMA determines that the balance of risks and benefits of using Translarna for the treatment of nmDMD has changed materially or that we have not or are unable to comply with any conditions that have been or may be placed on the marketing authorization, the European Commission could, at the EMA's recommendation, vary, suspend, withdraw or refuse to renew the marketing authorization for Translarna or require additional clinical trials or the imposition of other conditions or restrictions. If our marketing authorization in the EEA is not renewed, or our product label is materially restricted, we would lose all, or a significant portion of, our ability to generate revenue from product sales, whether pursuant to a commercial or an EAP program.

See "Risks Related to Regulatory Approval of our Product and our Product Candidates" below for further detail regarding conditional marketing authorizations in the EEA.

If clinical trials of our product or product candidates, such as our confirmatory Phase 3 clinical trials of Translarna, fail to demonstrate safety and efficacy to the satisfaction of the EMA, the FDA or other regulators, or do not otherwise produce favorable results, we may experience delays in completing, or ultimately be unable to complete, the development and commercialization of Translarna or any other product candidate.

In connection with seeking marketing authorization from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing authorization of their products.

The primary efficacy endpoint in the intent to treat, or ITT, population did not achieve statistical significance in the Phase 2b (completed in 2009) or Phase 3 ACT DMD (completed in 2015) clinical trials of Translarna for the treatment of nmDMD. Please review the foregoing risk factor titled, "*ACT DMD, our Phase 3 trial for Translarna for the treatment of nmDMD, did not meet its primary efficacy endpoint, and we received a Refuse to File letter from the FDA for our NDA submitted with data from this trial and the FDA recently denied our first appeal of the Refuse to File letter, the EMA is questioning the positive risk-benefit balance of Translarna for the treatment of nmDMD based on data from this trial and the CHMP has requested that we submit a proposal for a new clinical trial in nmDMD, and there is substantial risk that other regulators will not agree with our interpretation of the results of ACT DMD and the totality of clinical data from our trials in Translarna for the treatment of nmDMD, which would have a material adverse effect on our business, financial performance and results of operations*" for a review of recent developments that have had, and may continue to have, a material adverse effect on our ability to commercialize Translarna for the treatment of nmDMD, including: our receipt of a Refuse to File letter from the FDA with respect to our NDA for Translarna for the treatment of nmDMD; the FDA's recent denial of our appeal of the Refuse to File determination; the EMA's questioning of the positive risk-benefit balance of Translarna for the treatment of nmDMD, which is required in order for the CHMP to issue a positive opinion in favor of annual renewal of our marketing authorization to the European Commission; and the likelihood that if the CHMP issues a positive opinion in favor of the renewal of Translarna's

marketing authorization, such renewal, and any subsequent annual renewals, will be coupled with an obligation to conduct an agreed upon new clinical trial of Translarna for the treatment of nmDMD.

If the FDA, the EMA and other regulators do not agree with our interpretation of the results of the clinical data from our trials (including ACT DMD and related analyses) or otherwise view the results of these trials as favorable; if we are required to conduct additional clinical trials or other testing of Translarna or any other product candidate that we develop beyond those that we contemplate; if we are unable to successfully complete our clinical trials or other testing; if the results of these trials or tests are not positive or are only modestly positive; or if there are safety concerns, we may:

- be unable to successfully maintain or renew our current marketing authorization in the EEA for Translarna for the treatment of nmDMD, which is subject to annual review and renewal following reassessment of the risk-benefit balance of the authorization by the EMA;
- be delayed in obtaining additional marketing authorizations for Translarna for the treatment of nmDMD, for Translarna for the treatment of other indications or for our other product candidates;
- not obtain additional marketing authorizations at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements or restrictions;
- have the product removed from markets after obtaining applicable marketing authorizations; or
- not be permitted to sell Translarna under some or any reimbursed EAP programs.

If we or our collaborators experience any of a number of possible unforeseen events in connection with clinical trials related to our product or product candidates, including those under our collaboration with Roche and the SMA Foundation, potential marketing authorization or commercialization of our product or product candidates could be delayed or prevented.

We or our collaborators may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing authorization or commercialize our product or product candidates, including:

- clinical trials of our product or product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- we may be unable to enroll a sufficient number of patients in our trials to ensure adequate statistical power to detect any statistically significant treatment effects;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators, institutional review boards or independent ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site or may require us to submit additional data, conduct additional studies or amend our IND or comparable application prior to commencing a clinical trial;
- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- we may have to suspend or terminate clinical trials of our product or product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;

- regulators, institutional review boards or independent ethics committees may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;

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

- the supply or quality of our product or product candidates or other materials necessary to conduct clinical trials of our product or product candidates may be insufficient or inadequate; or

- our product or product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators, institutional review boards or independent ethics committees to suspend or terminate the trials.

For example, in the first half of 2015, dosing in the Phase 2 Moonfish study under our SMA collaboration was suspended and the study was placed on clinical hold to investigate an eye finding in a 39-week study in cynomolgus monkeys, which showed at exposures above those explored in SMA patients and healthy volunteers. The Moonfish trial is expected to be terminated during the fourth quarter of 2016. In October 2016, a two-part Phase 2 clinical study, called Sunfish, investigating the safety, tolerability and efficacy of a different product candidate under the SMA collaboration initiated in type 2 and type 3 SMA patients. While we and our collaboration partners intend to compare the profiles of each of these development compounds to determine the best path forward for the SMA program, this development has resulted in unanticipated delays in the advancement of the SMA program. In addition, we and our collaboration partners may need to perform additional studies, conduct further analyses, narrow the scope of the study, or take other actions to continue to advance the SMA program.

In addition, based on pre-clinical safety signals observed during the third quarter of 2015, we are no longer advancing PTC672 under our antibacterial program. Our product development costs will increase if we experience delays in testing or marketing authorizations. We do not know whether any preclinical tests or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product or product candidates, allow our competitors to bring products to market before we do, or impair our ability to successfully commercialize our product or product candidates, and so may harm our business and results of operations.

Our conclusions regarding the activity and potential efficacy of Translarna in nmDMD are primarily based on retrospective, subgroup and meta-analyses of the results of our Phase 2b and ACT DMD clinical trials of Translarna for the treatment of nmDMD. In addition, our conclusions regarding the activity and potential efficacy of Translarna in nmCF are primarily based on retrospective analyses of the results of our completed Phase 3 clinical trial of Translarna for nmCF. Other than with respect to certain of our meta-analyses, results of our analyses are expressed as nominal p-values, which are generally considered less reliable indicators of efficacy than adjusted p-values. In addition, retrospective analyses are generally considered less reliable than pre-specified analyses.

After determining that we did not achieve the primary efficacy endpoint with the pre-specified level of statistical significance in our completed ACT DMD and Phase 2b clinical trials of Translarna for the treatment of nmDMD, we performed subgroup, retrospective, and meta-analyses. On the basis of our position that the totality of clinical data from these trials support the clinical benefit of Translarna for the treatment of nmDMD, we submitted these analyses to the FDA, as part of our NDA. In addition, after determining that the primary efficacy endpoint did not achieve statistical significance in ACT DMD or our Phase 2b clinical trial of Translarna for the treatment of nmDMD and in our completed Phase 3 clinical trial of Translarna for nmCF, we performed retrospective and subgroup analyses that we believe provide strong support for concluding that Translarna was active and showed clinically meaningful improvements over placebo in these trials.

Although we believe that these additional analyses of the results of these trials were warranted, a retrospective analysis performed after unblinding trial results can result in the introduction of bias if the analysis is inappropriately tailored or influenced by knowledge of the data and actual results.

Some of our favorable statistical data from these trials also are based on nominal p-values that reflect only one particular comparison when more than one comparison is possible. A p-value is called nominal if it is the result of one particular comparison prior to any pre-specified multiplicity adjustment, such as when two active treatments are compared to placebo or when two or more subgroups are analyzed. For example, while the p-values for change from baseline at week 48 in the 6-minute walk test, or 6MWT, which we also refer to as 6-minute walk distance, or 6MWD, and each secondary end point timed function test in the pre-specified subgroup of ACT DMD patients with a baseline 300-400 meter 6MWD had p-values of less than 0.05, due to the sequential testing method, these p-values are considered nominal.

Typically, a trial result is statistically significant if the chance of it occurring when the treatment is like placebo is less than one in 20, resulting in a p-value of less than 0.05. Nominal p-values cannot be compared to the typical significance level (p-value less than 0.05) to determine statistical significance without being adjusted for the testing of multiple dose groups, end points or analyses of subgroups.

Because of these limitations, regulatory authorities typically give greater weight to results from pre-specified analyses and adjusted p-values and less weight to results from post-hoc, retrospective analyses and nominal p-values.

On February 22, 2016, we received a Refuse to File letter from the FDA stating that, in the view of the FDA, both the Phase 2b and Phase 3 ACT DMD trials were negative and do not provide substantial evidence of effectiveness and that our NDA does not contain adequate information regarding the abuse potential of Translarna. Additionally, the FDA stated that we had proposed a post-hoc adjustment of ACT DMD that eliminates data from a majority of enrolled patients. Our reliance on nominal p-values for some of our statistical data and our use of retrospective analyses had a negative impact on the FDA's view of our interpretation of the results of our Phase 2b trial, ACT DMD and the totality of data from our clinical trials. There is substantial risk that, notwithstanding any further dialogue we may be able to initiate with the agency, whether pursuant to continued appeal of the Refuse to File determination under the formal dispute resolution process or otherwise, the FDA will continue to disagree with our interpretation of our trial results and we may be required to perform additional clinical and non-clinical trials or complete additional analyses at significant cost, which, if successful, may enable FDA review of an NDA submission.

Our reliance on nominal p-values for some of our statistical data and our use of retrospective analyses has also had a negative impact on the EMA's evaluation of our applications for continued marketing authorization for Translarna for the treatment of nmDMD, including delays in timing of the CHMP's opinion with respect to the annual renewal of our marketing authorization, and could negatively impact regulatory determinations by regulators in other territories. As of the date of this filing, the EMA's CHMP has not issued an opinion with respect to our most recent request for renewal of our marketing authorization. In connection with our ongoing dialogue with the EMA with respect to the renewal of our marketing authorization, the CHMP issued a request for supplemental information, or RSI, in October 2016 that included a request classified as a major objection related to the efficacy and overall risk-benefit profile of Translarna as well as the design and conduct of an additional clinical trial that would provide comprehensive clinical data on these matters. Generally speaking, a failure to adequately address a major objection would preclude a recommendation for renewal of a marketing authorization. The extended duration of this renewal request cycle and some of the recent feedback we have received as part of the annual EMA reassessment process have introduced a greater degree of uncertainty as to whether we will receive a positive opinion from the CHMP. There is substantial risk that the EMA will not determine that the risk-benefit balance of Translarna supports renewal of our marketing authorization in the EEA, on the current approved label, or at all. If the EMA determines that the balance of risks and benefits of using Translarna for the treatment of nmDMD has changed materially or that we have not or are unable to comply with any conditions that have been or may be placed on the marketing authorization, the European Commission could, at the EMA's recommendation, vary, suspend, withdraw or refuse to renew the marketing authorization for Translarna.

With respect to our nmCF program, our use of retrospective and subgroup analyses diminishes the likelihood that the EMA will approve our request of a variation to our marketing authorization for Translarna to include Translarna for nmCF on a conditional basis and, even if we successfully complete ACT CF, could negatively impact the evaluation by the EMA and the FDA of our anticipated applications for full marketing authorization for Translarna for nmCF. In written feedback from the FDA in 2016 in connection with our Type C meeting request related to our ACT CF protocol, the FDA noted that statistically and clinically persuasive evidence from analyses of the primary and key secondary measures in ACT CF will be critical to support the effectiveness of Translarna for the treatment of nmCF, especially in the context of a single phase 3 study.

An unfavorable view of our data and analyses by the FDA and EMA for Translarna has and could continue to negatively impact our ability to obtain and maintain authorizations to market Translarna for the treatment of nmDMD or nmCF. An inability to obtain and maintain such marketing authorizations would have a material adverse effect on our anticipated revenue from Translarna and would materially harm our business, financial results and results of operations.

The results of ACT DMD and, even if successfully completed, the results of ACT CF, may not be sufficient for approval of Translarna for the applicable indication.

The primary efficacy endpoint in the intent to treat, or ITT, population did not achieve statistical significance in the Phase 2b (completed in 2009) or Phase 3 ACT DMD (completed in 2015) clinical trials of Translarna for the treatment of nmDMD. Please review the foregoing risk factor titled, "*ACT DMD, our Phase 3 trial for Translarna for the treatment of nmDMD, did not meet its primary efficacy endpoint, and we received a Refuse to File letter from the FDA for our NDA submitted with data*

from this trial and the FDA recently denied our first appeal of the Refuse to File letter, the EMA is questioning the positive risk-benefit balance of Translarna for the treatment of nmDMD based on data from this trial and the CHMP has requested that we submit a proposal for a new clinical trial in nmDMD, and there is substantial risk that other regulators will not agree with our interpretation of the results of ACT DMD and the totality of clinical data from our trials in Translarna for the treatment of nmDMD, which would have a material adverse effect on our business, financial performance and results of operations" for a review of recent developments that have had, and may continue to have, a material adverse effect on our ability to obtain or maintain marketing authorizations necessary to commercialize Translarna for the treatment of nmDMD in the United States, Europe and other territories, including our receipt of a Refuse to File letter from the FDA with respect to our NDA for Translarna for the treatment of nmDMD, the EMA's questioning of the risk-benefit balance of Translarna for the treatment of nmDMD and the CHMP's agreement to our proposal to submit for further discussion a draft clinical trial protocol regarding a new trial evaluating Translarna in nmDMD patients, which will include input from the EMA in the form of scientific advice.

Further, it is possible that, once completed and even if successful, the EMA or the FDA may not consider the results of ACT CF to be sufficient for approval of Translarna for such indication. The FDA typically requires two adequate and well-controlled pivotal clinical trials to support marketing authorization of a product candidate for a particular indication. The EMA or the FDA could determine that the results of our trials are not sufficiently robust, are subject to confounding factors, or are not adequately supported by other trial endpoints.

In addition, although we have had discussions with the FDA regarding ACT CF, the FDA may not consider our trial design acceptable. For example, in 2012, the FDA indicated that in its view the data from our completed Phase 3 clinical trial and other data from our development program in cystic fibrosis do not by themselves support an NDA submission and, consequently, the FDA informed us that additional clinical data would be required to establish the evidence necessary to support eventual filing of an NDA for the use of Translarna to treat nmCF. We had additional interactions with the FDA in 2013 regarding the clinical development design which would have the potential to support an NDA, but we did not achieve a consensus between the EMA and FDA views. Based on these interactions, we nonetheless initiated ACT CF in the first half of 2014 consistent with feedback from the EMA on our trial design.

While we have incorporated feedback we received from the FDA in 2012 and 2013 into our ACT CF trial design, we disagreed with two key recommendations: the designation of FEV_1, CF pulmonary exacerbations, and body mass index as three co-primary endpoints for the trial and a suggested three-year trial duration. Our ACT CF protocol continues to specify FEV_1 as the primary endpoint and each of pulmonary exacerbations, change from baseline BMI in patients, and health-related quality of life (respiratory domain), as secondary endpoints. We believe that these endpoints are consistent with other recent and ongoing clinical trials in cystic fibrosis and our earlier discussions with the FDA. In written feedback received from the FDA in 2016, while the agency acknowledged that we specified FEV_1 as our sole primary endpoint, the FDA noted that both statistically and clinically persuasive evidence from analyses of the primary and key secondary measures in ACT CF will be critical to support the effectiveness of Translarna, especially in the context of a single phase 3 study.

With respect to the FDA's 2013 advice concerning study duration, we continue to believe that a three-year trial would have resulted in a number of complications that ultimately would have limited the feasibility of the trial as well as the robustness of the data and conclusions that could be drawn from the results. In written feedback received from the FDA in 2016, the agency acknowledged that a 48-week trial may be of sufficient duration to demonstrate that Translarna improves FEV_1 versus placebo, while noting that this duration would likely not be sufficient to demonstrate that Translarna prevents FEV_1 decline compared to placebo. The FDA also noted in its 2016 feedback that prior increases to ACT CF patient enrollment, which we made in 2015 in light of data then available to us, should be addressed in any potential future NDA for Translarna for the treatment of nmCF. If the FDA does not ultimately consider our trial design for ACT CF acceptable, we may need to conduct more than one confirmatory clinical trial and our ability to receive marketing authorization for this indication could be delayed or prevented.

Because we are developing our product and our 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 the outcome of our clinical trials will not be favorable.

There are no marketed therapies approved to treat the underlying cause of nmDMD or nmCF. In addition, there has been limited historical clinical trial experience generally for the development of drugs to treat either of these diseases. As a result, the design and conduct of clinical trials for these diseases, particularly for drugs to address the underlying nonsense mutations causing these diseases in some subsets of patients, is subject to increased risk.

Prior to the Phase 2b clinical trial of Translarna for nmDMD, there was no precedent of an established trial design to evaluate the efficacy of Translarna in nmDMD over a 48 week duration. In addition, clinical understanding of the methodologies used to analyze the resulting data were also limited. The study design and enrollment criteria for ACT DMD were based on available

natural history data of the disease, including third party data and results from our Phase 2b clinical trial. An evolving understanding in the DMD community has led to a greater appreciation of the optimal window for the 6MWT in assessing physical function. We believe that this factor may have led to the primary efficacy endpoint in the intent to treat population not achieving statistical significance in ACT DMD.

With regard to nmCF, we believe that we now understand subgroup effects that we observed in our completed Phase 3 clinical trial and that we have designed our confirmatory Phase 3 ACT CF clinical trial of Translarna to take these effects into account. However, we may nonetheless experience unknown complications with ACT CF. As a result, we may not achieve the pre-specified endpoint with statistical significance in ACT CF, which would make approval of Translarna for this indication significantly more difficult to obtain.

We are faced with similar challenges in connection with the design of our Phase 2 proof-of-concept studies of Translarna in nmMPS I, nonsense mutation aniridia, and nonsense mutation Dravet syndrome/CDKL5 because there is also limited historical clinical trial experience for the development of drugs to treat the underlying cause of these disorders.

For example, with respect to nmMPS I, while clinical trials of enzyme replacement therapies conducted by third party sponsors have provided some insight into the disorder, enzyme replacement therapies do not sufficiently address the central nervous system, skeletal or cardiac symptoms associated with the disorder. In addition, our own pre-clinical and early stage clinical trials targeting nmMPS I have been limited in duration and, as a result, it is substantially uncertain whether our clinical design will optimize the duration or level of dosing or that we will be able to demonstrate a statistically significant biochemical or clinical effect in the primary or secondary pre-specified endpoints selected for the study.

If we experience delays or difficulties in the enrollment of patients in our clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates, including our confirmatory Phase 3 ACT CF clinical trial of Translarna or our Phase 2 proof-of-concept studies of Translarna in nmMPS I, nonsense mutation aniridia, or nonsense mutation Dravet syndrome/CDKL5, if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials. Patient enrollment will also be a critical factor as we seek scientific advice from the EMA with respect to our proposal to submit for further discussion a draft clinical trial protocol regarding a new trial evaluating Translarna in nmDMD patients. Each of these indications are characterized by relatively small patient populations, which could result in slow enrollment of clinical trial participants. In addition, our competitors have ongoing clinical trials for product candidates that could be competitive with our product candidates. As a result, potential clinical trial sites may elect to dedicate their limited resources to participation in our competitors' clinical trials and not ours, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

Patient enrollment is affected by other factors including:

- severity of the disease under investigation;
- eligibility criteria for the study in question;
- perceived risks and benefits of the product candidate under study;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

Enrollment delays in our clinical trials may result in increased development costs for our product candidates. Our inability to enroll a sufficient number of patients in our Phase 2 proof-of-concept studies of Translarna in nmMPS I, nonsense mutation aniridia, and nonsense mutation Dravet syndrome/CDKL5 or any of our other clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether.

For example, during the first quarter of 2015, we amended the study design for our proof-of-concept study for Translarna for the treatment of nmMPS I to include patients currently on enzyme replacement therapy. We anticipated that this change in

protocol might cause delays in patient enrollment, but expected that the larger addressable patient population would reduce the time to enroll the overall study. However, this protocol revision resulted in delays to site initiation and patient accrual, which in turn has delayed our expectations with respect to the timing of data from this study.

If serious adverse or inappropriate side effects are identified during the development of Translarna or any other product candidate, we may need to abandon or limit our development of that product or product candidate.

Our product and our product candidates are in clinical or preclinical development and their risk of failure is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. If our product or product candidates are associated with undesirable side effects or have characteristics that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause side effects that prevented further development of the compound.

For example, although we did not observe a pattern of liver enzyme elevations in our Phase 2 or Phase 3 clinical trials of Translarna, we did observe modest elevations of liver enzymes in some subjects in one of our Phase 1 clinical trials. These elevated enzyme levels did not require cessation of Translarna administration, and enzyme levels typically normalized after completion of the treatment phase. We did not observe any increases in bilirubin, which can be associated with serious harm to the liver, in the Phase 1 clinical trial.

In addition, in our completed Phase 3 clinical trial of Translarna for the treatment of nmCF, five adverse events in the Translarna arm of the trial that involved the renal system led to discontinuation. As compared to the placebo group, the Translarna treatment arm also had a higher incidence of adverse events of creatinine elevations, which can be an indication of impaired kidney function. In the Translarna treatment arm, more severe clinically meaningful creatinine elevations were reported in conjunction with cystic fibrosis pulmonary exacerbations. These creatinine elevations were associated with concomitant treatment with antibiotics associated with impaired kidney functions, such as aminoglycosides or vancomycin. This led to the subsequent prohibition of concomitant use of Translarna and these antibiotics, which was successful in addressing this issue in the clinical trial. If patients in the Translarna arm of a confirmatory Phase 3 clinical trial for the treatment of nmCF exhibit clinically meaningful creatinine elevations, the EMA or the FDA might not approve Translarna for this indication or could require that we instruct physicians to frequently monitor patients for these abnormalities or impose other conditions, which may be an impediment to the use of Translarna because of concerns related to its safety and convenience.

Our focus on the discovery and development of product candidates that target post-transcriptional control processes is unproven, and we do not know whether we will be able to develop products of any, or sustained, commercial value.

Our scientific approach focuses on the discovery and development of product candidates that target post-transcriptional control processes. While a number of commonly used drugs and a growing body of research validate the importance of post-transcriptional control processes in the origin and progression of a number of diseases, no existing drugs have been specifically designed to alter post-transcriptional control processes in the same manner as Translarna or our other product candidates. As a result, our focus on targeting these processes may not result in the discovery and development of commercially viable drugs that safely and effectively treat genetic disorders or other diseases. In addition, although we have received marketing authorization by the European Commission for Translarna for the treatment of nmDMD, such marketing authorization is subject to renewal pursuant to the annual EMA reassessment, our most recent request for annual renewal has not been granted at the time of this filing, there is substantial risk that the EMA will not determine that the risk-benefit balance of Translarna supports renewal of our marketing authorization, and, even if the EMA's CHMP determines to issue an opinion in favor of such renewal, we believe it is likely that such potential renewal, and any subsequent annual renewals, will be coupled with an obligation to conduct an agreed upon new clinical trial of Translarna for the treatment of nmDMD. We may not be successful in developing and receiving renewal of our marketing authorization or full regulatory authorization for such use and we may not receive regulatory approval for additional indications for Translarna or any other potentially commercially viable drug that treats an approved indication by targeting a particular post-transcriptional control process. Furthermore, we may not receive regulatory approval for product candidates that target different post-transcriptional control processes. If we fail to develop and commercialize viable drugs, we will not achieve commercial success.

Translarna for the treatment of nmDMD, or any other product candidate that receives marketing authorization, if any, may fail to achieve the degree of market acceptance by physicians, patients, third party payors and others in the medical community necessary for commercial success.

Although Translarna is currently authorized by the EMA for marketing for the treatment of nmDMD such marketing authorization is subject to annual renewal pursuant to the annual EMA reassessment and our most recent annual renewal request is subject to substantial risk and has not been granted at the time of this filing. Even if our marketing authorization in the EEA for Translarna for the treatment of nmDMD is maintained, or we are successful in obtaining marketing authorization for Translarna for other indications or territories or marketing authorization for any of our other product candidates, such product may nonetheless fail to gain sufficient market acceptance by physicians, patients, third party payors and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenues or any profits from operations. The degree of market acceptance of our product or product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments;
- the prevalence and severity of any side effects;
- the ability to offer our product or product candidates for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- sufficient third-party coverage or reimbursement; and
- any restrictions on concomitant use of other medications, such as a restriction that nmCF patients taking Translarna not also use chronic inhaled aminoglycoside antibiotics.

Our ability to negotiate, secure and maintain third-party coverage and reimbursement may be affected by political, economic and regulatory developments in the United States, the European Union and other jurisdictions. Governments continue to impose cost containment measures, and third-party payors are increasingly challenging prices charged for medicines and examining their cost effectiveness, in addition to their safety and efficacy. These and other similar developments could significantly limit the degree of market acceptance of Translarna for the treatment of nmDMD or any of our other product candidates that receive marketing authorization.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product or product candidates, we may not be successful in our continuing efforts to commercialize Translarna or commercializing any other product candidate if and when they are approved.

We have limited experience in the sale and marketing of pharmaceutical products, and we may be unable to successfully execute our commercial strategy in the EEA or, if approved, in the United States or other territories. Our commercial strategy for Translarna involves the development of a commercial infrastructure that spans multiple jurisdictions. Our ability to successfully commercialize Translarna for the treatment of nmDMD in the EEA and other territories, including the United States, if approved, is heavily dependent upon our ability to continue to build an infrastructure that is capable of implementing our global commercial strategy. International operations are subject to inherent risks. The establishment and development of our commercial infrastructure will continue to be expensive and time consuming, and we may not be able to develop our commercial organizations in all intended territories in a timely manner or at all. Doing so will require a high degree of coordination and compliance with laws and regulations in numerous jurisdictions, including restrictions on advertising practices, enforcement of intellectual property rights, restrictions on pricing or discounts, and unexpected changes in international regulatory requirements and tariffs. If we are unable to effectively coordinate such activities or comply with such laws and regulations, our ability to commercialize Translarna in those jurisdictions in which it is or may be approved will be adversely affected. If we are unable to establish and maintain adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate product revenue consistent with our expectations and may not become profitable.

We have evaluated markets outside of the EEA to determine in which geographies we might, if approved, choose to commercialize Translarna ourselves and in which geographies we might choose to collaborate with third parties. We intend to continue to promote Translarna for the treatment of nmDMD in permitted territories using both internal and external resources.

There are risks involved with establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training an internal commercial team is expensive and time consuming and could delay our commercialization efforts for Translarna for the treatment of nmDMD or any other product launch. If the commercial launch of Translarna or any other product candidate for which we recruit a commercial team and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition such personnel.

The arrangements that we have entered into, or may enter into, with third parties to perform sales and marketing services will generate lower product revenues or profitability of product revenues to us than if we were to market and sell any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively.

If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

Factors that may materially affect our efforts to commercialize our products on our own include:

- our ability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- our ability to implement third party marketing and distribution relationships on favorable terms, or at all, in territories where we do not pursue direct commercialization;
- the ability of our commercial team to obtain access to or persuade adequate numbers of physicians to prescribe Translarna or any future products;
- the lack of complementary products to be offered by our commercial team, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent commercial organization.

We plan to develop our commercial strategy for additional indications for Translarna or other product candidates, if and when such drugs are approved in the applicable region.

All of our sales of Translarna for the treatment of nmDMD currently occur in territories outside of the United States, which subjects us to additional business risks that could adversely affect our revenue and results of operations.

All of our revenue from sales of Translarna to date has been generated from countries other than the United States. We have operations in multiple European countries and other territories. We expect that we will continue to expand our international operations in the future, including in emerging growth markets, pending successful completion of the applicable regulatory processes. International operations inherently subject us to a number of risks and uncertainties, including:

- changes in international regulatory and compliance requirements that could restrict our ability to manufacture, market and sell our products;
- financial risks such as longer payment cycles, difficulty collecting accounts receivable and exposure to fluctuations in foreign currency exchange rates;
- difficulty in staffing and managing international operations;
- potentially negative consequences from changes in or interpretations of tax laws;
- changes in international medical reimbursement policies and programs;
- trade protection measures, including import or export licensing requirements and tariffs;
- our ability to develop relationships with qualified local distributors and trading companies;
- political and economic instability in particular foreign economies and markets, in particular in emerging markets;

- diminished protection of intellectual property in some countries outside of the United States;
- differing labor regulations and business practices; and
- regulatory and compliance risks that relate to maintaining accurate information and control over sales and distributors' and service providers' activities that may fall within the purview of the Foreign Corrupt Practices Act, UK Bribery Act or similar local regulation.

For example, we face risks arising out of the potential uncertainty caused by the recent vote in the United Kingdom in favor of exiting the European Union, commonly referred to as Brexit. Brexit could adversely affect European or worldwide political, regulatory, economic or market conditions and could contribute to instability in global political institutions, regulatory agencies and financial markets. Currency exchange rates in the pound sterling and the euro with respect to each other and the U.S. dollar have already been adversely affected by Brexit and, in the event that such foreign exchange volatility were to continue, it could cause volatility in our quarterly financial results. In addition, if the United Kingdom were to significantly alter its regulations affecting the pharmaceutical industry, we could face significant new regulatory costs and challenges.

In addition, some of the countries in which Translarna for the treatment of nmDMD is available for sale are in emerging markets and we anticipate that Translarna will become available to new emerging markets during 2016. Some countries within emerging markets may be especially vulnerable to periods of global or regional financial instability or may have very limited resources to spend on health care, including Brazil. We also may be required to increase our reliance on third-party agents within less developed markets. In addition, many emerging market countries have currencies that fluctuate substantially and if such currencies devalue and we cannot offset the devaluations, our financial performance within such countries could be adversely affected.

In addition, in some countries, including Brazil, orders for named patient sales are for multiple months of therapy, which can lead to an unevenness in orders which could result in significant fluctuations in quarterly net product sales. Other factors may also contribute to fluctuations in quarterly net product sales including Tranlarna's availability in any particular territory, government actions, economic pressures, political unrest and other factors. Net product sales are impacted by factors, such as the timing of decisions by regulatory authorities, in particular the FDA and the EMA with respect to our ability to market or sell Translarna for the treatment of nmDMD, and our ability to successfully negotiate favorable pricing and reimbursement processes on a timely basis in the countries in which we have or may obtain regulatory approval, including the United States, EEA and other territories.

Any of these factors may, individually or as a group, have a material adverse effect on our business and results of operations.

As we continue to expand our existing international operations, we may encounter new risks.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates and any products we may seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide.

There is currently no marketed therapy, other than Translarna in the EEA, which has received approval for the treatment of the underlying cause of nmDMD. Other currently available treatments for nmDMD are only palliative. Sarepta Therapeutics recently received approval in the United States for a treatment addressing the underlying cause of disease for different mutations in the DMD gene and other biopharmaceutical companies are developing treatments for Duchenne muscular dystrophy, including palliative treatments (Marathon Pharmaceuticals and Santhera Pharmaceuticals) and treatments addressing the underlying cause of disease for different mutations in the DMD gene (Daiichi Sankyo).

There are a number of large pharmaceutical and biotechnology companies that currently market and sell products to manage the symptoms and side effects of cystic fibrosis. These products include Novartis Pharmaceuticals Corporation's TOBI, Gilead Sciences, Inc.'s Cayston, and Genentech, Inc.'s Pulmozyme. Although there are currently no marketed products approved to treat the underlying cause of nmCF, Vertex Pharmaceuticals' drugs Kalydeco and Orkambi are approved by the FDA and in other territories as a treatment for cystic fibrosis caused by other mutations in the CFTR gene, not nonsense mutations. Vertex and other companies are developing other product candidates to treat cystic fibrosis for defined mutations or for all patients. We

believe that Translarna is the only product candidate in clinical trials that is designed to treat the underlying cause of nmCF by restoring CFTR activity.

Aldurazyme, which is manufactured by BioMarin Pharmaceutical Inc. and sold by Genzyme Corporation, is an enzyme replacement therapy for the treatment of mucopolysaccharidosis I. Furthermore, Diacomit is marketed in the European Union by Laboratoires Biocodex for the treatment of Dravet's syndrome. Other companies are also pursuing product candidates for the treatment of Dravet's syndrome, including GW Pharmaceuticals and Insys Therapeutics. Aniridia therapeutic interventions, such as artificial iris implantation, are being developed by HumanOptics AG. Our SMA collaboration with Roche and the SMA Foundation also faces competition. For example, Ionis Pharmaceuticals, Inc. and Biogen recently submitted a NDA to the FDA for its antisense product candidate as a treatment for SMA. AveXis, Inc. is also evaluating a gene therapy product candidate for the treatment of SMA. Other companies are also pursuing product candidates for the treatment of SMA, including Novartis Pharmaceuticals Corporation.

Our competitors may develop products that are more effective, safer, more convenient or less costly than any that we are developing or that would render our product candidates obsolete or non-competitive. Our competitors may also obtain marketing authorization for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

We believe that many competitors are attempting to develop therapeutics for the target indications of our product candidates, including academic institutions, government agencies, public and private research organizations, large pharmaceutical companies and smaller more focused companies.

Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to or necessary for our programs.

Even if we are able to commercialize Translarna for the treatment of nmDMD on a broad scale or commercialize Translarna for other indications or any other product candidate that we develop, the product may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

We currently expect that Translarna will be priced at levels consistent with the pricing for other therapies for the treatment of rare disorders where high unmet medical need exists.

The regulations and practices that govern marketing authorizations, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries, including almost all of the member states of the EEA, require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, including the European market, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing authorization for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing authorization.

Our ability to commercialize Translarna or any other product candidate successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the EU and U.S. healthcare industries and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Prices at which we or our customers seek reimbursement for our products can be subject to challenge, reduction or denial by the government and other payers. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure

that coverage and reimbursement will be available for Translarna or any other product that we commercialize and, if coverage and reimbursement are available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing authorization. Obtaining reimbursement for Translarna may be particularly difficult because of the higher prices typically associated with drugs directed at smaller populations of patients. In addition, third-party payors are likely to impose strict requirements for reimbursement of a higher priced drug. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing authorization.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the applicable regulatory authority. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs, and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. In the United States, third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. In addition, there has been recent negative publicity and Congressional scrutiny around pharmaceutical drug pricing in the U.S. Moreover, U.S. government authorities and third-party payors are increasingly attempting to limit or regulate drug prices and reimbursement, particularly for new and innovative therapies. These dynamics may give rise to negative reactions to pricing decisions for products for which we may receive regulatory approval in the future, possibly limiting our ability to generate revenue and attain profitability. In the European Union, reference pricing systems and other measures may lead to cost containment and reduced prices. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition. In addition, in the European Union, for medicines authorized by the centralized authorization procedure, an authorized trader, such as a wholesaler, can purchase a medicine in one EU member state and import the product into another EU member state. This process is called “parallel distribution”. As a result, a purchaser in one EU member state may seek to import Translarna from another EU member state where Translarna is sold at a lower price. This could have a negative impact on our business, financial condition, results of operations and growth.

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

We face an inherent risk of product liability exposure related to the commercialization of Translarna, any other product that we may commercialize, and in connection with the human clinical trials testing of our product candidates and the sales of our products, including Translarna and any other product that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- reduced resources of our management to pursue our business strategy;
- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- increased insurance costs, or an inability to maintain appropriate insurance coverage;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

We have product liability insurance that covers our commercial sales, sales pursuant to reimbursed EAP programs and clinical trials up to a $25.0 million annual aggregate limit, and subject to a per claim deductible. The amount of insurance we currently hold may not be adequate to cover all liabilities and defense costs that we may incur. We may need to further increase our insurance coverage as we continue commercializing Translarna or as and when we begin commercializing any other product candidate that receives marketing authorization. The cost of insurance coverage is highly variable, based on a wide range of factors, and 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 or defense costs 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 handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations currently, and may in the future, involve the use of hazardous and flammable materials, including chemicals and medical and biological materials, and produce hazardous waste products. Even if we 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 or disposal of hazardous wastes, we could be held liable for any resulting damages, and any liability could exceed our resources.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We also maintain liability insurance for some of these risks, but our liability policy excludes pollution and has an aggregate coverage limit of $11.0 million.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and product candidates for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. For example, we initiated separate Phase 2 clinical trials of Translarna for the treatment of hemophilia in 2009 and the metabolic disorder methylmalomic acidemia in 2010, but then suspended these clinical trials to focus on the development of Translarna for nmDMD and nmCF when we found variability in the assays used in these trials and preliminary data from these trials did not indicate definitive evidence of activity. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products.

We have based our research and development efforts on small-molecule drugs that target post-transcriptional control processes. Notwithstanding our large investment to date and anticipated future expenditures in proprietary technologies, including GEMS and our alternative splicing technology, which we use in the discovery of these molecules, to date we have only been granted marketing authorization to treat nmDMD under a restricted label, and subject to the fulfillment of certain conditions and ongoing renewal requirements, in the EEA. We may not be able to successfully renew or satisfy the ongoing requirements of our current marketing authorization for nmDMD and we may never successfully develop any other marketable drugs or indications using our scientific approach. As a result of pursuing the development of product candidates using our proprietary technologies, we may fail to develop product candidates or address indications based on other scientific approaches that may offer greater commercial potential or for which there is a greater likelihood of success. Research programs to identify new product candidates require substantial technical, financial and human resources. These research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development.

If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Risks Related to our Dependence on Third Parties

We contract with third parties for the manufacture and distribution of our product and our product candidates, which may increase the risk that we will not have sufficient quantities of our products or product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our commercialization or development efforts.

We do not own or operate manufacturing or distribution facilities for the production or distribution of clinical or commercial supplies of our product candidates. We have limited personnel with experience in drug manufacturing and lack the resources and the capabilities to manufacture any of our product candidates on a clinical or commercial scale. We currently rely on third parties for supply of the active pharmaceutical ingredients in Translarna and all of our product candidates. We outsource all manufacturing, packaging, labeling and distribution of our products and product candidates to third parties, including our commercial supply of Translarna.

We currently have a contract with a pharmacy and hospital distributor in the European Union that distributes Translarna for clinical programs and limited commercial and EAP programs. We have engaged with third party logistic providers, or 3PLs, which distribute Translarna for the majority of our commercial and EAP programs on our behalf. We intend to engage additional distributors if and when, if ever, we become authorized to make Translarna available for purchase in such additional geographies.

We currently rely on a single source for the production of some of our raw materials and we obtain our supply of the bulk drug substance for Translarna from two third-party manufacturers and the bulk drug substance for our cancer stem cell program through another third-party manufacturer. We engage a separate manufacturer to provide bulk drug product and expect to finalize our validation of another bulk drug manufacturer in 2016. We have a relationship with two manufacturers that are capable of providing fill and finish services for our finished commercial and clinical product, although we are still in the process of finalizing arrangements with one of these manufacturers with respect to commercial product services. During 2016, we anticipate engaging a third manufacturer to provide fill and finish services for both commercial and clinical product. We do not currently have any agreements with third-party manufacturers for the long-term commercial supply of Translarna or any of our product candidates. We expect to engage in discussions with certain third-party suppliers and manufacturers with respect to commercial supply agreements for Translarna bulk drug substance and product during 2016.

We may be unable to conclude agreements for commercial or clinical supply with third-party manufacturers, or may be unable to do so on acceptable terms.

Even if we are able to establish and maintain arrangements with third-party manufacturers and distributors, reliance on such service providers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how;
- the possibility of commercial supplies of Translarna not being distributed to commercial vendors or end users in a timely manner, resulting in lost sales;
- the possibility of clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Many additional factors could cause production or distribution interruptions with the manufacture and distribution of Translarna and any of our product candidates, including human error, natural disasters, labor disputes, acts of terrorism or war, equipment malfunctions, contamination, or raw material shortages.

In addition, third-party manufacturers or distributors may not be able to comply with current good manufacturing practice, or cGMP, or good distribution practice, or GDP, or similar regulatory requirements outside the European Union and the United States. Our failure, or the failure of our third-party manufacturers or distributors, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or product, operating restrictions, criminal prosecutions or debarment, any of which could significantly and adversely affect supplies of Translarna or our product candidates.

Our product and our product candidates and any other products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

If the third parties that we engage to manufacture product for our commercial sales, preclinical tests and clinical trials should, prior to the time that we have validated alternative providers, cease to continue to do so for any reason, we likely would experience delays in our ability to supply Translarna to patients or in advancing our clinical trials while we identify and qualify replacement suppliers and we may be unable to obtain replacement supplies on terms that are favorable to us. In addition, if we are not able to obtain adequate supplies of Translarna or our product candidates or the drug substances used to manufacture them, we will lose commercial sales revenue and it will be more difficult for us to develop our product candidates and compete effectively.

Our current and anticipated future dependence upon others for the manufacture and distribution of Translarna and our product candidates may adversely affect our business, financial condition, results of operations and growth including our ability to develop product candidates and commercialize our products that receive regulatory approval on a timely and competitive basis.

We rely on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We do not independently conduct clinical trials for our product or product candidates. We rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to perform this function. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for clinical development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as Good Clinical Practices, or GCP, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. Similar GCP and transparency requirements apply in the European Union. Failure to comply with such requirements, including with respect to clinical trials conducted outside the European Union and United States, can also lead regulatory authorities to refuse to take into account clinical trial data submitted as part of a marketing application.

For example, in the first half of 2013 inspectors acting at the request of the EMA conducted GCP inspections of selected clinical sites from our completed Phase 2b clinical trial of Translarna for the treatment of nmDMD and our clinical trial site relating to our then pending marketing authorization application, or MAA, for approval of Translarna for the treatment of nmDMD. Following these inspections, we received inspection reports containing a combination of critical and major findings. These findings related to waivers we granted to admit patients to our Phase 2b clinical trial of Translarna for the treatment of nmDMD in advance of formal approval of protocol amendments that would have established their eligibility for the trial, as well as our oversight of our trial sites and the completeness or sufficiency of clinical trial documentation. In response to these findings, we described to the EMA the enhanced internal procedures and controls we have implemented, and the internal quality assurance department we have established, since the conclusion of our Phase 2b clinical trial of Translarna for the treatment of nmDMD. In addition, we proposed corrective action plans to address the inspectors' specific findings. If we do not meet our commitment to the corrective actions we proposed to the EMA, we may face additional consequences, including rejection of data or other direct action by national regulatory authorities, which could require us to conduct additional clinical trials or other supportive studies to maintain our marketing authorization in the EEA for Translarna for the treatment of nmDMD or to obtain full approval from the EMA.

Furthermore, third parties that we rely on for our clinical development activities may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing authorizations for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. Our product development costs will increase if we experience delays in testing or obtaining marketing authorizations.

We also rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing authorizations of our product or product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

We currently depend, and expect to continue to depend, on collaborations with third parties for the development and commercialization of some of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

For each of our product candidates, we plan to evaluate the merits of retaining commercialization rights for ourselves or entering into selective collaboration arrangements with leading pharmaceutical or biotechnology companies, such as our collaborations with Roche and the SMA Foundation, for our spinal muscular atrophy program. We have entered into arrangements with certain third parties to market or distribute Translarna for the treatment of nmDMD in certain countries and, as we continue to implement our commercialization plans for Translarna, we anticipate that we will engage additional third parties to perform these functions for us in other countries. We generally plan to seek collaborators for the development and commercialization of product candidates that have high anticipated development costs, are directed at indications for which a potential collaborator has a particular expertise, or involve markets that require a large sales and marketing organization to serve effectively. Our likely collaborators for any marketing, distribution, development, licensing or broader collaboration arrangements may include: large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and/or biotechnology companies.

We will have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' desire and ability to successfully perform the functions assigned to them in these arrangements. In particular, the successful development of a product candidate from our spinal muscular atrophy program will initially depend on the success of our collaborations with the SMA Foundation and Roche, including whether Roche continues clinical development of the current clinical candidate or pursues clinical development of any other compounds identified under the collaborations.

Collaborations involving our product candidates, including our collaborations with the SMA Foundation and Roche, pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs, based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise between the collaborator and us as to the ownership of intellectual property arising during the collaboration;

- we may grant exclusive rights to our collaborators, which would prevent us from collaborating with others;

- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and

- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

Collaborators have terminated collaborations with us in the past. For example, in 2008, we entered into a collaboration with Genzyme Corporation for the development and commercialization of Translarna under which we granted to Genzyme rights to commercialize Translarna in all countries other than the United States and Canada. In 2011, we restructured the collaboration and regained worldwide rights to Translarna, with Genzyme obtaining an option to commercialize Translarna in indications other than nmDMD outside the United States and Canada. In 2012, this option expired without being exercised by Genzyme and the collaboration terminated.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

If we are not able to establish additional collaborations, we may have to alter our development and commercialization plans.

Our product development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate further with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborators' resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborators' evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge; and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under future license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

If we fail to comply with our obligations in our intellectual property licenses and funding arrangements with third parties, we could lose rights that are important to our business.

We are a party to a number of license agreements and expect to enter into additional licenses in the future. Our existing licenses impose, and we expect that future licenses will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, the licensor may have the right to terminate the license, in which event we might not be able to market any product that is covered by these agreements, which could materially adversely affect the value of the product candidate being developed under such license agreement. Termination of these license agreements or reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms, or cause us to lose rights in important intellectual property or technology.

We have also received grant funding for some of our development programs from philanthropic organizations and patient advocacy groups pursuant to agreements that impose development and commercialization diligence obligations on us. If we fail to comply with these obligations, the applicable organization could require us to grant to the organization exclusive rights under certain of our intellectual property, which could materially adversely affect the value to us of product candidates covered by that intellectual property even if we are entitled to a share of any consideration received by such organization in connection with any subsequent development or commercialization of the product candidates.

Some of our patented technology was developed with U.S. federal government funding. When new technologies are developed with U.S. government funding, the government obtains certain rights in any resulting patents, including a nonexclusive 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 patented 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 U.S. government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations or to give preference to U.S. industry. In addition, U.S. government-funded inventions must be reported to the government and U.S. government funding must be disclosed in any resulting patent applications. Furthermore, our rights in such inventions are subject to government license rights and certain restrictions on manufacturing products outside the United States.

Risks Related to our Intellectual Property

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

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products. We seek to protect our proprietary position by filing patent applications in the United States and in certain foreign jurisdictions related to our novel technologies, product and product candidates that are important to our business. This process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, if we license technology or product candidates from third parties in the future, these license agreements may not permit us to control the preparation, filing and prosecution of patent applications, or to maintain or enforce the patents, covering this intellectual property. These agreements could also give our licensors the right to enforce the licensed patents without our involvement, or to decide not to enforce the patents at all. Therefore, in these circumstances, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. 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 products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, patent law in many countries restricts the patentability of methods of treatment of the human body more than U.S. law does. In addition, we may not pursue or obtain patent protection in all major markets. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. In addition, the Leahy-Smith America Invents Act of 2011 (the "Act"), which reformed certain patent laws in the U.S., may create additional uncertainty. The significant changes engendered by the Act include switching from a "first-to-invent" system to a "first-to-file" system, and the implementation of new procedures that permit competitors to challenge our patents in the USPTO after grant, including inter partes review and post grant review.

Moreover, we may be subject to a third party anonymously submitting prior art to a patent office or may become involved in addressing patentability objections based on third party submission of references, oppositions, derivation proceedings, reexamination, inter partes review, post grant review, interference proceedings or other patent office proceedings or litigation, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize our product or current or future product candidates.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. In addition, other companies may attempt to circumvent any regulatory data protection or market exclusivity that we obtain under applicable legislation, which may require us to allocate significant resources to preventing such circumvention. Legal and regulatory developments in the European Union and elsewhere may also result in clinical trial data submitted as part of an MAA becoming publicly available. The EMA Policy on publication of clinical data, as well as the current application of European Union freedom of information regulations, could impact our proprietary information (comprising both clinical and non-clinical data) that would normally be maintained by a regulatory body as confidential. Such developments could enable other companies to circumvent our intellectual property rights and use our clinical trial data to obtain marketing authorizations in the European Union and in other jurisdictions. Such developments may also require us to allocate significant resources or engage in litigation to prevent other companies from circumventing or violating our intellectual property rights. Our attempts to prevent third parties from circumventing our intellectual property and other rights may ultimately be unsuccessful. We may also fail to take the required actions or pay the necessary fees to maintain our patents.

For example, during 2015, we were notified by the EMA that it had received from another pharmaceutical company a request under Regulation (EC) No 1049/2001 seeking access to aspects of our Translarna MAA. Following the decision of the EMA to release such documentation with only minimal redactions we have initiated litigation before the General Court of the European Union to prevent disclosure of this information, and in July 2016, the Court took the interim measure of ordering the EMA to not release our documents until the substantive case has been decided (by the General Court or in possible appeal proceedings). The EMA has appealed the General Court's decision on interim measures to the Court of Justice of the European Union and the appeal proceedings are ongoing. While we expect to continue to object to the disclosure of any information that we consider commercially confidential, there can be no assurance that we will be successful in the aforementioned litigation or in any future challenge that may be raised and we may not ultimately be successful in preventing disclosure of the data in our MAA.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged on such a basis in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

Competitors may infringe our patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their intellectual property or defenses, such that they do not infringe our intellectual property. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question.

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

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product and our product candidates and use our proprietary technologies without infringing the intellectual property and other proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference, derivation, inter partes review or post-grant review proceedings before the U.S. Patent and Trademark Office. The risks of being involved in such litigation and proceedings may also increase as our product candidates approach commercialization, and as we gain greater visibility as a public company. Third parties may assert infringement claims against us based on existing or future intellectual property rights. We may not be aware of all such intellectual property rights potentially relating to our product and our product candidates. Since 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, with new publications occurring continuously, there may be patents or patent applications relating to our product or our product candidates that we are unaware of. There may also be pending or future patent applications that, if issued, would block us from commercializing Translarna. Thus, we do not know with certainty whether Translarna, or any of our other product candidates, or our commercialization thereof, would or would not infringe any third party's intellectual property.

If we are found to infringe a third party's intellectual property rights, or in order to avoid or settle litigation, we could be required to obtain a license to continue developing and marketing our products 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 access to the same technologies licensed to us, and could require us to make substantial payments. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys fees if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from commercializing our product or our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

For example, it is possible that one or more third parties might bring a patent infringement or other legal proceeding against us regarding Translarna. We are aware of an issued U.S. patent and international patent applications that purport to disclose or contain claims to chemical scaffolds that are sufficiently broad that they could be read to encompass ataluren, the active ingredient in Translarna, even though neither the issued U.S. patent nor any of the international patents or patent applications specifically discloses ataluren. In order to successfully challenge the validity of any issued U.S. patent that may allegedly include ataluren within the scope of a granted claim, we would need to overcome that patent's presumption of validity in district court or prove unpatentability by a preponderance of the evidence before the USPTO. There is no assurance that a court or the USPTO would find these claims to be invalid or unpatentable, respectively. In addition, we believe that the public notice given by our testing of ataluren in clinical trials for the purpose of seeking FDA approval would be a valid defense against any infringement claims in the United States based on the availability of any statutory research exemptions. However, there can be no assurance that our interpretation of the exemption would be upheld, were the exemption interpreted as covering only our preclinical research activities, and not the commercialization of ataluren.

We may be subject to claims by third parties asserting that we or our employees have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees 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 do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

In addition, while we typically require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.
If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

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

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. 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, 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. 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.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. However, we cannot guarantee that we have executed these agreements with each party that may have or have had access to our trade secrets or that the agreements we have executed will provide adequate protection. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be obtained or independently developed by a competitor, our competitive position would be harmed.

We have not yet registered our trademarks in all of our potential markets, and failure to secure those registrations could adversely affect our business.

Our trademark applications may be refused registration, and our registered trademarks may not be maintained or found to be enforceable. During trademark examination proceedings, our trademark applications may be rejected. Although we are given an opportunity to respond to those rejections, we may not be able to overcome them. In addition, in the U.S. Patent and Trademark Office and Trademark Offices in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. In addition, if we do not secure registrations for our trademarks, we may encounter difficulty enforcing our trademark rights against third parties.

If we are not able to obtain adequate trademark protection or regulatory approval for our brand names, including Translarna, we may be required to re-brand affected products, which could cause delays in getting such products to market and substantially increase our costs.

To protect our rights in any trademark we intend to use for our product or our product candidates, including Translarna, we may seek to register such trademarks. Trademark registration is territory-specific and we must apply for trademark registration in the United States as well as any other country where we intend to commercialize our product or product candidates. Failure to obtain trademark registrations may place our use of the trademarks at risk or make them subject to legal challenges, which could force us to choose alternative names for our product or product candidates. In addition, the FDA, and other regulatory authorities outside the United States, typically conduct an independent review of proposed product names for pharmaceuticals, including an evaluation of the potential for confusion with other product names for medications, which could result in prescribing errors. These regulatory authorities may also object to a proposed product name if they believe the name inappropriately makes or implies a therapeutic claim. If the FDA or other regulatory authorities outside the United States object to any of our proposed product names, we may be required to adopt alternative names for our product or product candidates. If we adopt alternative names, either because of our inability to obtain a trademark registration or because of objections from regulatory authorities, we would lose the benefit of our existing trademark applications and the rights attached thereto.

Consequently, we may be required to expend significant additional resources in an effort to adopt a new product name that would be registrable under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA and other regulatory authorities, which could cause delays in getting our products to market and substantially increase our costs. Furthermore, we may not be able to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our ability to commercialize our product or our product candidates.

Risks Related to Regulatory Approval of our Product and our Product Candidates

Our marketing authorization in the EEA requires annual renewal by the European Commission, which, as of the date of this filing, has not been granted, and there is substantial risk that the EMA will not determine that the risk-benefit balance of Translarna supports renewal of our marketing authorization, on the current label, or at all, and, even if the European Commission grants renewal of our marketing authorization, such renewal will likely be conditioned upon the results of a not yet designed trial for Translarna for the treatment of nmDMD, which will likely result in significant expense and uncertainty for us. If we are not able to obtain renewal of our marketing authorization, we will not be able to continue to commercialize Translarna for nmDMD and our ability to generate revenue will be materially impaired.

We received initial marketing authorization for Translarna for the treatment of nmDMD in ambulatory patients aged five years and older from the European Commission in August 2014 as a "conditional marketing authorization." The marketing authorization is subject to annual review and renewal by the European Commission following reassessment by the EMA of the risk-benefit balance of the authorization and our ability to implement measures, including pharmacovigilance plans, that are detailed in the risk management plan, and, when granted, was further conditioned upon our submission of the final clinical study report, including additional efficacy and safety data, from ACT DMD. We submitted the ACT DMD report to the EMA in January 2016 as a type II variation request, which sought to have the specific condition to our marketing authorization removed and a full marketing authorization granted. In February 2016, we also submitted a marketing authorization renewal request with the EMA. As of the date of this filing, the EMA's CHMP has not issued an opinion with respect to our most recent request for renewal of our marketing authorization.

For additional information regarding risks related to the results of ACT DMD, including our interactions with the EMA with respect to the ACT DMD report, see the risk factor under "Risks Related to the Development and Commercialization of our Product and our Product Candidates" titled, "*ACT DMD, our Phase 3 trial for Translarna for the treatment of nmDMD, did not meet its primary efficacy endpoint, and we received a Refuse to File letter from the FDA for our NDA submitted with data from this trial and the FDA recently denied our first appeal of the Refuse to File letter, the EMA is questioning the positive risk-benefit balance of Translarna for the treatment of nmDMD based on data from this trial and the CHMP has requested that we submit a proposal for a new clinical trial in nmDMD, and there is substantial risk that other regulators will not agree with our interpretation of the results of ACT DMD and the totality of clinical data from our trials in Translarna for the treatment of nmDMD, which would have a material adverse effect on our business, financial performance and results of operations.*"

Conditional marketing authorizations based on incomplete clinical data, including our marketing authorization for Translarna for the treatment of nmDMD, may be granted for a limited number of listed medicinal products for human use, including products designated as orphan medicinal products under EU law, if (1) the EMA determines that the risk-benefit balance of the product is positive, (2) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (3) unmet medical needs will be fulfilled and (4) the benefit to public health of the immediate availability on the market of the medicinal product outweighs the risk inherent in the fact that additional data are still required. Specific obligations or conditions, including with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data, may be specified in the conditional marketing authorization. Marketing authorizations subject to conditions are only valid for one year, and must be renewed annually by the European Commission after an assessment by the EMA of the ongoing positive risk-benefit balance in favor of continued authorization and the need for additional or modified conditions.

We had previously anticipated that the EMA's CHMP would issue an opinion with respect to our type II variation and annual renewal submissions requests related to marketing authorization continuation by mid-2016. As of the date of this filing, the EMA's CHMP has not issued an opinion with respect to the renewal of our marketing authorization, although we expect that the committee's opinion as to whether the risk-benefit balance of treatment favors ongoing authorization will be issued in 2016. While the EMA has not formally declined our type II variation request for full approval of our marketing authorization, we believe that it is unlikely that the EMA will recommend in favor of this request.

Following conclusion of an oral explanation meeting with the CHMP in October 2016, the CHMP issued a request for supplementary information, or RSI, with a request classified as a major objection. As with prior RSIs we received during this most recent marketing authorization renewal and variation request process, the major objection relates to the efficacy and

overall risk-benefit profile of Translarna as well as the design and conduct of an additional clinical trial that would provide comprehensive clinical data demonstrating a robust and clinically meaningful effect of Translarna in a nmDMD patient population which would confirm the positive risk-benefit ratio of Translarna and address outstanding uncertainties about efficacy. The CHMP has noted in previous RSIs that this trial must be deemed feasible in the post-authorization setting. Generally speaking, a failure to adequately address a major objection would preclude a recommendation for renewal of a marketing authorization. The most recent RSI also includes requests categorized as other concerns, which do not rise to the level of a major objection, and are generally associated with long-term risk and labeling matters as well as the primary pharmacology of Translarna.

The extended duration of this renewal request cycle and some of the recent feedback we have received as part of the annual EMA reassessment process have introduced a greater degree of uncertainty as to whether we will receive a positive opinion from the CHMP. The CHMP may issue a negative opinion against renewal of the marketing authorization on the basis that, in the committee's view, the balance of risks and benefits of using Translarna for the treatment of nmDMD has changed materially. In such an event the European Commission could, at the EMA's recommendation, vary, suspend, withdraw or refuse to renew the marketing authorization for Translarna.

There is substantial risk that the EMA will not determine that the risk-benefit balance of Translarna supports renewal of our marketing authorization in the EEA, on the current approved label, or at all. We believe that if the CHMP determines to issue a positive opinion in favor of renewing our annual marketing authorization, such renewal, and any subsequent annual renewals, will be coupled with an obligation to conduct an agreed upon new clinical trial of Translarna for the treatment of nmDMD. Designing, enrolling, conducting and completing a clinical trial is a time-consuming, expensive and uncertain process that takes years to complete, and we expect that we will incur material ongoing costs related to the development of such a trial in the short-term, as well as the implementation of the trial in the longer term.

The EMA may also impose other new conditions to our marketing authorization (in addition to the potential new clinical trial described above), and may make other recommendations, including new label restrictions. In the event that we do secure annual renewal of the marketing authorization this year, the EMA could nevertheless later determine that we have not complied, or are unable to comply, with any conditions that have been or may be placed on the marketing authorization, which again could result in the withdrawal of our marketing authorization or other outcome that would have a materially adverse effect on our business.

If our marketing authorization in the EEA is not renewed, or our product label is materially restricted, we would lose all, or a significant portion of, our ability to generate revenue from product sales, whether pursuant to a commercial or an EAP program, which would have a material adverse effect on our business, financial results and operations.

The FDA denied our first appeal of the Refuse to File letter we received from the agency regarding our NDA for Translarna for the treatment of nmDMD, there is substantial risk that we will not be successful in further appeals of the Refuse to File letter to progressively higher levels of the FDA, and by determining to continue to pursue our appeal under the formal dispute resolution process with the FDA, we have postponed other available strategic pathways which may have proven to be more effective. If there are delays in obtaining regulatory approval in the United States, we will not be able to commercialize Translarna for nmDMD in that territory and our ability to generate revenue will be materially impaired.

On October 17, 2016, we announced that the FDA denied our first appeal of the agency's decision to issue a Refuse to File letter with respect to our NDA for Translarna for the treatment of nmDMD. Our appeal of the FDA's Division of Neurological Products' refusal to review our NDA is being conducted in accordance with the formal dispute resolution process that exists within the FDA's Center for Drug Evaluation and Research.

Although we intend to continue our appeal of the Refuse to File determination to progressively higher levels of FDA management under the ongoing formal dispute resolution process, we expect that our efforts to resolve the matters set forth in the Refuse to File letter, whether pursuant to this appeal or otherwise, will be time-consuming and may be expensive. In addition, there is significant risk that the FDA will not reverse its Refuse to File decision and review of our NDA for Translarna for nmDMD in a timely fashion, or at all. For example, we filed a formal dispute resolution request with the FDA in connection with the agency's refuse to file our NDA submitted for approval of Translarna for the treatment of nmDMD that was based on our Phase 2b data. In January 2012, the FDA reaffirmed the appropriateness of its earlier decision to refuse to file the 2011 NDA. In the current Refuse to File letter, the FDA referenced its prior refusal to file relative to the Phase 2b data and our discussions with the FDA, reiterating the views previously disclosed.

Even if we are successful in reversing the Refuse to File decision, there is significant risk that we will be unable to obtain FDA approval of Translarna for nmDMD, on a timely basis or at all, and we may be required to perform additional clinical and non-

clinical trials or analyses at significant cost which, if we if are able to enroll and fund and if successful, may enable FDA review of an NDA submission by us and, ultimately, may support approval of Translarna for nmDMD in the U.S.

Furthermore, by determining to pursue formal dispute resolution, we have postponed other strategic pathways, such as requesting that our NDA be filed over protest with the FDA, commencing direct litigation, or discussing the design of a new clinical trial with the FDA. Such alternative strategies may have proven to be more effective in achieving our ultimate goal of approval for Translarna for the treatment of nmDMD in the United States. We will not be able to commercialize Translarna for nmDMD in the United States until we have obtained regulatory approval from the FDA. Delays in obtaining such approval will materially impair our ability to generate revenue from Translarna for the treatment of nmDMD.

For additional information on ACT DMD, please review the risk factor under "Risks Related to the Development and Commercialization of our Product and our Product Candidates" titled, "*ACT DMD, our Phase 3 trial for Translarna for the treatment of nmDMD, did not meet its primary efficacy endpoint, and we received a Refuse to File letter from the FDA for our NDA submitted with data from this trial and the FDA recently denied our first appeal of the Refuse to File letter, the EMA is questioning the positive risk-benefit balance of Translarna for the treatment of nmDMD based on data from this trial and the CHMP has requested that we submit a proposal for a new clinical trial in nmDMD, and there is substantial risk that other regulators will not agree with our interpretation of the results of ACT DMD and the totality of clinical data from our trials in Translarna for the treatment of nmDMD, which would have a material adverse effect on our business, financial performance and results of operations.*"

If we are not able to comply with local regulations for our product or product candidates, we will not be able to obtain or maintain product approvals and commercialize our product or product candidates, and our ability to generate revenue will be materially impaired.

Translarna and our product candidates, and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and EMA and by comparable authorities in other countries. Failure to obtain marketing authorization for Translarna or any product candidate will prevent us from commercializing such product or product candidate.

As noted in the foregoing risk factors, we may not receive necessary approvals from the FDA, the EMA, or other regulators to further commercialize Translarna for nmDMD or to commercialize Translarna for any other indication or commercialize any product candidate in any market.

We have not proven our ability to successfully obtain marketing authorizations to sell our product or product candidates, other than with respect to the marketing authorization granted by the European Commission in August 2014 for Translarna for the treatment of nmDMD, which is subject to annual review and renewal following reassessment of the risk-benefit balance of the authorization by the EMA and satisfaction of any conditions that may be imposed by the EMA (and our most recent request for marketing authorization renewal is pending as of the time of this filing and subject to substantial risk) and the marketing authorizations granted in Israel and South Korea (which are largely contingent upon continued EMA approval). We have begun seeking and intend to continue to seek marketing authorization for Translarna for the treatment of nmDMD in territories outside of the EEA. There is substantial risk that regulators in other territories will not agree with our interpretation of the results of ACT DMD and the totality of clinical data from our trials, which would have a material adverse effect on our ability to generate revenue from the sales of Translarna for the treatment of nmDMD in those territories.

In addition, during the third quarter of 2015 we submitted a variation to our marketing authorization application with the EMA to seek to include Translarna for the treatment of nmCF, and based on recent interactions with the CHMP, we believe that the results from our ongoing ACT CF trial may be required before the CHMP issues an opinion with respect to this type II variation request and we no longer expect final resolution of this matter in 2016. There is substantial risk that the EMA will not grant us approval of Translarna for the treatment of nmCF. We expect that even if the EMA approves a variance to include Translarna for nmCF, the EMA will require us, as a post-approval measure, to provide it with comprehensive clinical data from ACT CF. In addition, unless and until we satisfy the conditions of our primary marketing authorization in the EEA for Translarna (for the treatment of nmDMD), any potential future authorization of Translarna for the treatment of nmCF would continue to be subject to annual review and renewal by the European Commission following reassessment by the EMA. In the event that the European Commission determined not to renew our marketing authorization for Translarna for the treatment of nmDMD, we would be required to submit a separate marketing authorization application to the EMA and European Commission for approval of Translarna for the treatment of nmCF, which would significantly delay our ability to market and sell Translarna in the EEA, if ever.

We have only limited experience in filing and supporting the applications necessary to obtain marketing authorizations for product candidates and expect to continue to rely on third-party contract research organizations to assist us in this process. Securing marketing authorization requires the timely preparation and submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. In response to changes in the regulatory environment or requests from regulators, we may elect, or be obliged, to postpone a regulatory submission to include additional analyses, including those intended to strengthen our submission or facilitate regulator review, which could cause delays in getting our products to market and substantially increase our costs. Securing marketing authorization also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Regulatory authorities may determine that Translarna or any of our other product candidates are not effective or only moderately effective, or have undesirable or unintended side effects, toxicities, safety profiles or other characteristics that preclude us from obtaining marketing authorization or that prevent or limit commercial use.

The process of obtaining marketing authorizations is expensive, may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing authorization policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing authorization of a product candidate. Any marketing authorization we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable. For example, the marketing authorization granted on a conditional basis by the EMA in the EEA for Translarna is limited to ambulatory nmDMD patients aged five years and older who have been identified through genetic testing.

In addition, marketing authorizations in countries outside the United States do not ensure pricing approvals in those countries or in any other countries, and marketing authorizations and pricing approvals do not ensure that reimbursement will be obtained.

We may not be able to obtain orphan drug exclusivity for our product candidates. If our competitors are able to obtain orphan drug exclusivity for their products that are the same drug as our product candidates, or can be classified as a similar medicinal product within the meaning of EU law, 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 European Union and the United States, may designate drugs for relatively small patient populations as orphan drugs. We have obtained orphan drug designations from the EMA and from the FDA for Translarna for the treatment of nmDMD, nmCF, nmMPS I, and nonsense mutation aniridia. Generally, if a product with an orphan drug designation subsequently receives the first marketing authorization for the indication for which it has such designation, the product is entitled to a period of market exclusivity, which, subject to certain exceptions, precludes the EMA from accepting another marketing application for a similar medicinal product or the FDA from approving another marketing application for the same drug for the same indication for that time period. The applicable market exclusivity period is ten years in the European Union and seven years in the United States. The EU exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation, including if the drug is sufficiently profitable so that market exclusivity is no longer justified. However, in the European Union, generic medicinal products that rely on the independently generated data submitted as part of a full marketing authorization application dossier of an authorized medicinal product, a "reference product", may not be placed on the market for 10 years from the granting of the initial marketing authorization for the reference product.

In the European Union, a "similar medicinal product" is a medicinal product containing a similar active substance or substances as contained in a currently authorized orphan medicinal product, and which is intended for the same therapeutic indication. For a drug such as Translarna, which is composed of small molecules, the FDA defines "same drug" as a drug that contains the same active moiety and is intended for the same use. Obtaining orphan drug exclusivity for Translarna for these indications, both in the European Union and in the United States, may be important to the product candidate's success. If a competitor obtains orphan drug exclusivity for and approval of a product with the same indication as Translarna before we do and if the competitor's product is the same drug or a similar medicinal product as ours, we could be excluded from the market. Even if we obtain orphan drug exclusivity for Translarna for these indications, we may not be able to maintain it. For example, if a competitive product that is the same drug or a similar medicinal product as Translarna is shown to be clinically superior to our product candidate, any orphan drug exclusivity we have obtained will not block the approval of such competitive product. In addition, orphan drug exclusivity will not prevent the approval of a product that is the same drug as Translarna if the FDA finds

that we cannot assure the availability of sufficient quantities of the drug to meet the needs of the persons with the disease or condition for which the drug was designated. The same considerations would apply to any of our orphan product candidates.

All pharmaceutical products for which marketing authorization has been granted, including Translarna for the treatment of nmDMD in the EEA, are subject to extensive and rigorous governmental regulation and could be subject to restrictions or withdrawal from the market and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

We, Translarna, our product candidates, our operations, our facilities, our suppliers, and our contract manufacturers, distributors, and contract testing laboratories are subject to extensive regulation by governmental authorities in the EEA, the United States, and other territories, with regulations differing from country to country.

We are not permitted to market our product candidates in the EEA, the United States, or other territories until we have received requisite regulatory approvals. In order to receive and maintain such approvals, we and our third-party service providers must comply on a continuous basis with a broad array of regulations related to establishment registration and product listing, manufacturing processes, risk management measures, quality and pharmacovigilance systems, pre- and post-approval clinical data, labeling, advertising and promotional activities, record keeping, distribution, and import and export of pharmaceutical products for any product for which we obtain marketing authorization. Any regulatory approval of any of our products or product candidates, once obtained, may be withdrawn. For example, our marketing authorization in the EEA is subject to annual renewal pursuant to the EMA reassessment process, which, as of the time of this filing, has not been granted and is subject to substantial risk. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing and distribution. For additional information with respect to the risks related to renewal of our marketing authorization in the EEA, see the foregoing risk factor titled "*Our marketing authorization in the EEA requires annual renewal by the European Commission, which, as of the date of this filing, has not been granted, and there is substantial risk that the EMA will not determine that the risk-benefit balance of Translarna supports renewal of our marketing authorization, on the current label, or at all, and, even if the European Commission grants renewal of our marketing authorization, such renewal will likely be conditioned upon the results of a not yet designed trial for Translarna for the treatment of nmDMD, which will likely result in significant expense and uncertainty for us. If we are not able to obtain renewal of our marketing authorization, we will not be able to continue to commercialize Translarna for nmDMD and our ability to generate revenue will be materially impaired.*"

We are required to submit safety and other post-market information and reports, implement pharmacovigilance plans, and comply with cGMP requirements related to manufacturing including, quality control, quality assurance and complaints and corresponding maintenance of records and documents, requirements regarding the distribution of samples to healthcare professionals and recordkeeping, among other things, in connection with the marketing authorization for Translarna for the treatment of nmDMD described above. Regulatory authorities, including the EMA and local regulatory authorities in EEA member states, subject a marketed product, its manufacturer and the manufacturing facilities to ongoing review and periodic inspections and the EMA is responsible for coordinating inspections, undertaken by the competent authorities of applicable member states, of our manufacturing facilities to assess whether our manufacturing, and other procedures, comply with cGMP. Similar regulatory and inspection requirements apply in other jurisdictions including those imposed by the FDA in the United States.

Even if marketing authorization of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or may be subject to significant conditions of approval, including the requirement of risk evaluation and mitigation strategy, or REMS. A regulatory authority also may impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. In addition, the competent authorities of each EU member state and the FDA closely regulate the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling and regulatory requirements. Such regulatory authorities can impose stringent restrictions on manufacturers' communications regarding off-label use and if we do not comply with the laws governing promotion of approved drugs, we may be subject to enforcement action for off-label promotion. Violations of the Federal Food, Drug, and Cosmetic Act relating to the promotion of prescription drugs may lead to civil and criminal penalties, investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results which could negatively affect our business, including:

- restrictions on such products, manufacturers or manufacturing processes;

- changes to or restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to implement a REMS;
- requirements to conduct post-marketing studies or clinical trials;
- warning or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing authorizations;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions;
- the imposition of civil or criminal penalties; or
- debarment.

Non-compliance with EU requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

We are also subject to laws and license and registration requirements covering the distribution of marketed products. If we fail to comply with any of these requirements, we may be subject to action by regulatory agencies, which could negatively affect our business. Regulatory agencies may also change existing requirements or adopt new requirements or policies. We may be slow to adapt or may not be able to adapt to these changes or new requirements.

Our initial commercial launch of Translarna has begun in, and is expected to continue to take place in, countries that tend to impose strict price controls, which may adversely affect our revenues, if any. Failure to obtain and maintain acceptable pricing and reimbursement terms for Translarna in the European Economic Area and other jurisdictions would prevent us from marketing our products in such regions.

In some countries, particularly the member states of the EEA, the pricing of prescription pharmaceuticals is subject to strict governmental control. Each country in the EEA has its own pricing and reimbursement regulations and may have other regulations related to the marketing and sale of pharmaceutical products in the country. We generally will not be able to commence commercial sales of Translarna for the treatment of nmDMD pursuant to the marketing authorization granted by the European Commission in any particular member state of the EEA until we conclude the applicable pricing and reimbursement negotiations and comply with any licensing, employment or related regulatory requirements in that country. In some countries we may be required to conduct additional clinical trials or other studies of our product including trials that compare the cost-effectiveness of our product to other available therapies in order to obtain reimbursement or pricing approval. We may not be able to conclude pricing and reimbursement negotiations or comply with additional regulatory requirements in the countries in which we seek to commercialize Translarna on a timely basis, or at all.

The pricing and reimbursement process varies from country to country and can take over 18 months to complete. Pricing negotiations may continue after reimbursement has been obtained. We cannot predict the timing of Translarna's commercial

launch in countries where we are awaiting pricing and reimbursement guidelines. While we have submitted pricing and reimbursement dossiers with respect to Translarna for the treatment of nmDMD in other key EEA countries, we have only received both pricing and reimbursement approval on terms that are acceptable to us in a limited number of countries.

In addition, the price that is approved by local governmental authorities pursuant to commercial pricing and reimbursement processes may be significantly lower than the price we are able to charge for sales under our reimbursed early access programs. In some instances, reimbursement may be subject to challenge, reduction or denial by the government and other payers. In some countries, such as France, EAP and commercial sales of a product can begin while pricing and reimbursement rates are under discussion with the applicable government health programs. In the event that the negotiated price of the product is lower than the amount reimbursed for sales made prior to the conclusion of price negotiations, the company may become obligated to repay such excess amount to the applicable government health program. We will make such retroactive reimbursement, if any, following the conclusion of price negotiations with the applicable government health authority.

For example, based on unsustainable economics imposed by the arbitration board in Germany upon the recent conclusion of an arbitration process with us and the German Federal Association of the Statutory Health Insurances (GKV-Spitzenverband), we delisted Translarna from the German pharmacy ordering system, effective April 1, 2016. Under these circumstances, patients and healthcare professionals in Germany have been able to access Translarna through a reimbursed importation pathway possible under German law, however, there can be no assurance that all of such patients will be successful in such an endeavor or, if initially successful, that any or all will continue to be successful. While we were permitted under local law to sell product on a commercial basis for the one-year period commenced December 2014 while market access discussions were held, we were and continue to be required to reimburse payors in Germany the difference between the commercial price of Translarna and the price established by the arbitration board in Germany for sales made in Germany since December 2015, other than sales made pursuant to the reimbursed importation pathway.

Political, economic and regulatory developments may further complicate pricing and reimbursement negotiations and there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. For example, we have been engaged in market access discussions with National Health Services (NHS) England since 2014. During the fourth quarter of 2014, NHS England determined to reconsider how it assesses certain new treatments and postponed certain pricing and reimbursement meetings, including meetings related to Translarna, and in July 2015 determined that final funding decisions on Translarna for nmDMD would be made after the conclusion of a specialized appraisal process by the National Institute for Health and Care Excellence, or NICE. In July 2016, NICE issued final guidance recommending Translarna for nmDMD patients within the EMA-approval label when used in connection with a five-year managed access agreement entered into by PTC, NICE, NHS England as well as the NorthStar clinical network and the patient organisations Muscular Dystrophy UK and Action Duchenne. The managed access agreement establishes the clinical details surrounding the use of Translarna, including the terms and conditions of a confidential financial arrangement and the collection of further data on the efficacy of Translarna for the treatment of nmDMD over a five-year period with NICE guidance to be reviewed again at the end of that period, before future funding decisions are taken.

In addition, adverse clinical and regulatory developments may exacerbate these risks, including the developments noted in the foregoing risk factor titled, "*ACT DMD, our Phase 3 trial for Translarna for the treatment of nmDMD, did not meet its primary efficacy endpoint, and we received a Refuse to File letter from the FDA for our NDA submitted with data from this trial and the FDA recently denied our first appeal of the Refuse to File letter, the EMA is questioning the positive risk-benefit balance of Translarna for the treatment of nmDMD based on data from this trial and the CHMP has requested that we submit a proposal for a new clinical trial in nmDMD, and there is substantial risk that other regulators will not agree with our interpretation of the results of ACT DMD and the totality of clinical data from our trials in Translarna for the treatment of nmDMD, which would have a material adverse effect on our business, financial performance and results of operations.*"

Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. Publication of discounts by third-party payors or authorities may lead to further pressure on prices or reimbursement levels within the country of publication and other countries.

If we fail to successfully secure and maintain pricing and reimbursement coverage for Translarna or are significantly delayed in doing so or if burdensome conditions are imposed by private payers, government authorities or other third-party payers on such reimbursement, planned launches in the affected countries will be delayed and our anticipated revenue and growth prospects could be negatively affected and our business could be adversely affected.

Our relationships with customers, healthcare providers and professionals and third-party payors are or will be subject to applicable anti-kickback, fraud and abuse, transparency and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any products or product candidates, including Translarna. Our arrangements with customers, healthcare providers and professionals and third-party payors may expose us to broadly applicable fraud and abuse, transparency and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing authorization.

Failure to maintain a comprehensive and effective compliance program, and to integrate the operations of any acquired businesses into a combined comprehensive and effective compliance program on a timely basis, could subject us to a range of regulatory actions that could affect our ability to commercialize our products and could harm or prevent sales of the affected products, or could substantially increase the costs and expenses of commercializing and marketing our products.
Restrictions and reporting requirements under applicable federal and state healthcare laws and regulations, and equivalent laws and regulations in the European Union, include, and are not limited to, the following:

- Anti-corruption and anti-bribery statutes, including the U.S. Foreign Corrupt Practices Act, or FCPA, and the UK Bribery Act of 2010, or Bribery Act. These statutes are generally broad in scope and will require us to make and keep books and records that accurately and fairly reflect the transactions of the company and to devise and maintain an adequate system of internal accounting controls. The FCPA prohibits the offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to improperly influence any act or decision, secure any other improper advantage, or obtain or retain business. Under the UK Bribery Act, companies which carry on a business or part of a business in the United Kingdom may be held liable for bribes given, offered or promised to any person, including non-UK government officials and private persons, by employees and persons associated with the company in order to obtain or retain business or a business advantage for the company. Other countries have adopted, or may adopt in the future, similar anti-corruption and anti-bribery statutes with which we may be required to comply.

- Anti-kickback statutes, which generally prohibit, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under government funded healthcare programs. The U.S. federal statute has been broadly interpreted to apply to manufacturer arrangements with prescribers, purchasers and formulary managers, among others and many states have enacted equivalent state laws that apply not only to government payors but commercial payors. Several other countries, including the United Kingdom, have enacted similar anti-kickback, fraud and abuse, and healthcare laws and regulations.

- The Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively the Affordable Care Act), amended the intent requirement of the federal anti-kickback statute such that a person no longer needs to have actual knowledge of the statue or specific intent to violate it. 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 U.S. False Claims Act.

- The Affordable Care Act also added a provision requiring certain providers and suppliers of services to Federal Health Care Programs to report and return overpayments within sixty days after they are “identified” (the “Overpayment Statute”). In February 2016, the Centers for Medicare and Medicaid Services (“CMS”) released long-awaited regulatory guidance (in the form of a final rule) to Medicare Part A and Part B providers and suppliers regarding how to comply with the Overpayment Statute. CMS had previously released a final rule addressing overpayments involving Medicare Part C and Part D providers in May 2014. Although Medicare Part A/B/C/D providers and suppliers have faced federal False Claims Act liability since 2010 for failures to comply with the Overpayment Statute, these final rules interpreting the Overpayment Statute provide guidance to providers and suppliers regarding how to comply appropriately with applicable obligations, and guidance to government regulators and enforcement authorities regarding monitoring and prosecuting suspected violations. Although not directly applicable to us, this final rule may impact our customers and potential customers who are Medicare providers and suppliers.

- Laws and regulations, including the U.S. False Claims Act, which impose civil and criminal liability on individuals and entities who submit, or cause to be submitted, false or fraudulent claims for payment to the government. The U.S. government has brought False Claims Act actions against pharmaceutical companies on the theory that their practices have caused false claims to be submitted to the government. The U.S. Attorneys’ Offices and the main Department of Justice have taken broad interpretations of what constitutes falsity or false claims. A wide range of pharmaceutical

manufacturers' commercial activity, marketing practices and price reporting practices have been scrutinized as potential violations of the False Claims Act.

- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program. HIPAA also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information, and imposes criminal and civil liability for violations of these obligations. In addition, international data protection laws including the European Union Data Protection Directive and member state implementing legislation may apply to some or all of the clinical data obtained outside of the United States. Furthermore, certain privacy laws and genetic testing laws may apply directly to our operations and/or those of our collaborators and may impose restrictions on our use and dissemination of individuals' health information.

- HIPAA also imposes criminal liability for knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services.

- Laws and regulations regulating off-label promotion. Off-label promotion of medicinal products is prohibited in the European Union. The applicable laws at European Union 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 European Union 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. Under the Federal Food, Drug and Cosmetic Act and other laws, if any of our product candidates are approved, we would be prohibited from promoting our products for off-label uses. This means, for example, that we would not be able to make claims about the use of our marketed products outside of their approved indications, and we would not be able to proactively discuss or provide information on off-label uses of such products, with very specific and limited exceptions. The FDA does not, however, restrict physicians from prescribing products for off-label uses in the practice of medicine. Should the FDA determine that our activities constituted the promotion of off-label use, the FDA could bring action to prevent us from distributing those products for the off-label use and could impose fines and penalties on us and our executives.

- Statutory requirements to disclose publicly payments made to physicians, including in certain EU member states and the United States. For example, in the U.S., under the federal Physician Payments Sunshine Act requirements, manufacturers of drugs, devices, biologics and medical supplies must report information related to payments and other transfers of value made to or at the request of covered recipients, such as physicians and teaching hospitals, as well as physician ownership and investment interests in such manufacturers. A number of states have enacted their own transparency requirements that obligate manufacturers to report different types of spending related to physicians and other covered recipients.

- Laws governing the advertising and promotion of medicinal products, interactions with physicians and patients, misleading and comparative advertising and unfair commercial practices. For example, legislation adopted by individual EU member states that may apply to the advertising and promotion of medicinal products require that promotional materials and advertising in relation to medicinal products comply 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. Promotion of indications not covered by the SmPC is specifically prohibited.

- Analogous state laws and regulations, such as state anti-kickback, false claims and privacy laws, may apply to our sales or marketing arrangements, claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, or other activities. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures.

In addition, interactions between pharmaceutical companies and physicians are also governed by industry self-regulation codes of conduct and physicians' codes of professional conduct. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the European Union. The provision of benefits or advantages to physicians is also governed by the national laws of the EU member states, as well as codes of conduct issued by self-regulatory industry bodies. Moreover, agreements with physicians

must often be the subject of prior notification and approval by the physician's employer, their competent professional organization, and the competent 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.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws, regulations, transparency requirements and self-regulatory codes will involve substantial costs. We cannot guarantee that we, our employees, our consultants or our third-party contractors are or will be in compliance with all federal, state and foreign regulations and codes. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, reputational harm, and the curtailment or restructuring of our operations. Exclusion, suspension and debarment from government funded healthcare programs would significantly impact our ability to commercialize, sell or distribute any drug. 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 also have an adverse effect on our business, financial condition and results of operations. If
any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing authorization of and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing authorization of Translarna or any of our other product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates, including Translarna, for which we obtain marketing authorization.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or Medicare Modernization Act, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act may result in a similar reduction in payments from private payors.

In March 2010, President Obama signed into law the Affordable Care Act, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Effective October 1, 2010, the Affordable Care Act revised the definition of "average manufacturer price" for reporting purposes, which could increase the amount of Medicaid drug rebates to states. Further, the new law imposes a significant annual fee on companies that manufacture or import branded prescription drug products.

There have been multiple attempts through legislative action and legal challenge to repeal or amend the Affordable Care Act. Although the U.S. Supreme Court in King v. Burwell upheld the use of subsidies to individuals in federally facilitated health care exchanges on June 25, 2015, which ultimately did not disrupt significantly the implementation of the Affordable Care Act, we cannot predict whether other current or future efforts to repeal or amend these laws will be successful, nor can we predict the impact that such a repeal or amendment would have on our business and operations, or on our results of operations. In addition, there are numerous steps required to implement the Affordable Care Act, and implementation remains ongoing. Congress also has enacted, and may continue to seek, legislative changes that alter, delay, or eliminate some of its provisions. On February 1, 2016, the Centers for Medicare and Medicaid Services released a long-awaited new rule, the Medicaid Program Covered Outpatient Drug Final Rule, effective April 1, 2016, implementing various provisions of the Affordable Care Act related to "covered outpatient drugs," including revising the calculation of "average manufacturer price" and addressing other issues relating to Medicaid price reporting and reimbursement. These and other changes contribute to the uncertainty of the ongoing implementation and impact of the Affordable Care Act; they also underscore the potential for additional reform going forward. Certain provisions of enacted or proposed legislative changes may negatively impact coverage and reimbursement of healthcare items and services. We cannot assure that the Affordable Care Act, as currently enacted or as amended in the future,

will not adversely affect our business and financial results and we cannot predict how future federal or state legislative or administrative changes relating to healthcare reform will affect our business.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing authorizations of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing authorization, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize Translarna and our product candidates. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our chief executive officer and other key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on Dr. Stuart W. Peltz, our co-founder and Chief Executive Officer, and the other principal members of our executive and scientific teams. Although we have formal employment agreements with each of our executive officers, these agreements do not prevent our executives from terminating their employment with us at any time. We do not maintain "key person" insurance on any of our executive officers. The loss of the services of any of these persons might impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

We are in the process of expanding our development, regulatory, and sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

In connection with our commercialization plans and business strategy, including our commercial launch of Translarna for the treatment of nmDMD, we have experienced and may to continue to experience significant growth in our employee base for sales, marketing, operational, managerial, financial, human resources, drug development, quality, regulatory and medical affairs and other areas. This growth has imposed and will continue to impose significant added responsibilities on members of management, including the need to recruit, hire, retain, motivate and integrate additional employees. Also, our management may have to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. To manage our recent and anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Risks Related to our Common Stock

Servicing the Convertible Notes will require a significant amount of cash. We may not have sufficient cash flow from our business to make payments on our debt, and we may not have the ability to raise the funds necessary to settle conversions of, or to repurchase, the Convertible Notes upon a fundamental change, which could adversely affect our business, financial condition and results of operations.

In August 2015, we incurred indebtedness in the amount of $150.0 million in aggregate principal with additional accrued interest under the Convertible Notes, for which interest is payable semi-annually in arrears on February 15 and August 15 of each year, beginning on February 15, 2016. Our ability to make scheduled payments of the principal of, to pay interest on or to refinance the Convertible Notes depends on our future performance, which is subject to economic, financial, competitive and other factors beyond our control. Our business may not generate cash flow from operations in the future sufficient to service our debt, including the Convertible Notes. If we are unable to generate cash flow, we may be required to adopt one or more alternatives, such as selling assets, restructuring debt or obtaining additional equity capital on terms that may be unfavorable to us or highly dilutive. Our ability to refinance our indebtedness will depend on the capital markets and our financial condition at the time we seek to refinance such indebtedness. We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations.

In addition, upon conversion of the Convertible Notes unless we elect to deliver solely shares of our common stock to settle such conversion (other than paying cash in lieu of delivering any fractional shares), we will be required to make cash payments in respect of the Convertible Notes being converted. However, we may not have enough available cash or be able to obtain financing at the time we are required to repurchase Convertible Notes, to pay the Convertible Notes at maturity or to pay cash upon conversions of Convertible Notes. In addition, our ability to repurchase Convertible Notes or to pay cash upon conversions of Convertible Notes may be limited by law, by regulatory authority or by agreements governing our future indebtedness. Our failure to repurchase Convertible Notes at a time when the repurchase is required by the indenture, to make interest payments on the Convertible Notes when due under the indenture or to pay any cash payable on future conversions of the Convertible Notes as required by the indenture would constitute a default under the indenture. An event of default under the indenture governing the Convertible Notes or the fundamental change itself could also lead to a default under agreements governing our future indebtedness. If the repayment of any such related indebtedness were to be accelerated after any applicable notice or grace periods, we may not have sufficient funds to repay the indebtedness, repurchase the Convertible Notes, make interest payments on the Convertible Notes or make cash payments upon conversions of the Convertible Notes.

In addition, even if holders of the Convertible Notes do not elect to convert their Convertible Notes, we could be required under applicable accounting rules to reclassify all or a portion of the outstanding principal of the Convertible Notes as a current rather than long-term liability, which would result in a material reduction of our net working capital. Any of these factors could materially and adversely affect our business, financial condition and results of operations.

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 our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- provide for a classified board of directors such that 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 “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.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock and lawsuits against us and our officers and directors.

Our stock price has been and will likely continue to be volatile. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our stockholders may not be able to sell their common stock at or above the price at which they purchased it. The market price for our common stock may be influenced by many factors, including:

- any developments related to our ability or inability to resolve the matters set forth in the Refuse to File letter we received from the FDA in connection with our NDA for Translarna for the treatment of nmDMD, including matters related to our appeal of the Refuse to File decision by the FDA under the formal dispute resolution process and whether we will be required to complete any additional clinical and non-clinical trials or analyses;
- whether the EMA determines that the risk-benefit balance of Translarna supports renewal of our marketing authorization in the EEA, on the current approved label, or at all;
- any developments related to any clinical trial for Translarna for the treatment of nmDMD that may be developed with input from the EMA, including with respect to design, timing, conduct, and enrollment, and developments with respect to any clinical or nonclinical trial that may be required by other regulatory agencies, including the FDA for Translarna for the treatment of nmDMD;
- other developments concerning our regulatory submissions with the EMA for Translarna for the treatment of nmDMD and for the treatment of nmCF;
- whether regulators in other territories agree with our interpretation of the results of ACT DMD;
- our ability to advance the commercialization of Translarna for the treatment of nmDMD;
- the success of competitive products or technologies;
- results of clinical trials of Translarna, in particular ACT CF, and any other product candidate that we develop;
- the development and regulatory status of our SMA program with Roche and the SMA Foundation;
- results of clinical trials of product candidates of our competitors;
- 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;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;

- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

Companies that have experienced volatility in the market price of their stock have frequently been the subject of securities class action and shareholder derivative litigation. See Part II, Item 1. Legal Proceedings in this Quarterly Report on Form 10-Q for information concerning litigation initiated against us and certain of our officers during the first quarter of 2016. In addition, we could be the target of other such litigation in the future. Class action and derivative lawsuits, whether successful or not, could result in substantial costs, damage or settlement awards and a diversion of our management’s resources and attention from running our business, which could materially harm our reputation, financial condition and results of operations.

We are currently incurring and expect to continue to incur increased costs as a result of operating as a public company, including compliance with Section 404 of the Sarbanes-Oxley Act of 2002, and our management is and will continue to be required to devote substantial time to compliance initiatives. In addition, the failure to establish and maintain adequate finance infrastructure and accounting systems and controls could impair our ability to comply with the financial reporting and internal controls requirements for publicly traded companies.

As a public 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, the Dodd-Frank Act, the listing requirements of The NASDAQ Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel have and will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have and will continue to increase our legal and financial compliance costs and will continue to make some activities more time-consuming and costly. For example, these rules and regulations have made it more difficult and more expensive for us to obtain director and officer liability insurance.

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 the effectiveness of our internal control over financial reporting and an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. Compliance with Section 404, including documentation and evaluation of our internal control over financial reporting, is both costly and challenging. If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner each year, we could be subject to sanctions or investigations by the Securities and Exchange Commission, the NASDAQ Stock Market or other regulatory authorities which would require additional financial and management resources and could adversely affect the market price of our common stock. Furthermore, if we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed and investors could lose confidence in our reported financial information.

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

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the development and growth 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 our stockholders sole source of gain for the foreseeable future.

Sales of a substantial number of shares of our common stock in the public market by our existing stockholders could significantly reduce the market price of our common stock.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock.

We have issued a significant number of equity awards under our equity compensation plans or as inducement grants to new hire employees pursuant to Nasdaq rules. The shares underlying these awards are or, with respect to certain option grants, will be registered on a Form S-8 registration statement. As a result, upon vesting these shares can be freely exercised and sold in the public market upon issuance, subject to volume limitations applicable to affiliates. The exercise of options and the subsequent

sale of the underlying common stock or the sale of restricted stock upon vesting could cause a decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

Certain of our employees, executive officers and directors 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 or director. A Rule 10b5-1 plan may be amended or terminated in some circumstances. Our employees, executive officers and directors may also buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

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

Recent Sales of Unregistered Securities

Inducement stock option awards. Pursuant to the NASDAQ inducement grant exception, during the quarter ended September 30, 2016, we issued options to purchase an aggregate of 22,900 shares of common stock to certain new hire employees at a weighted-average exercise price of $8.29 per share. The shares underlying these option awards will be registered on a Form S-8 registration statement prior to the first vesting event applicable to each such award.

Item 6. Exhibits.

Those exhibits required to be filed by Item 601 of Regulation S-K are listed in the Exhibit Index immediately preceding the exhibits hereto and such listing is incorporated herein by reference.

SIGNATURES

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

PTC THERAPEUTICS, INC.

Date: November 2, 2016

By: /s/ Shane Kovacs

Shane Kovacs

Chief Financial Officer

(Principal Financial and Accounting Officer and Duly Authorized Signatory)

EXHIBIT INDEX

Exhibit Number	Description of Exhibit
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1	Certification of Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS	XBRL Instance Document*
101.SCH	XBRL Taxonomy Extension Schema Document*
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document*
101.LAB	XBRL Taxonomy Extension Label Linkbase Database*
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document*
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document*

* Submitted electronically herewith.

Exhibit 31.1

CERTIFICATIONS

I, Stuart W. Peltz, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of PTC Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 2, 2016

By: /s/ STUART W. PELTZ

Stuart W. Peltz
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Shane Kovacs, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of PTC Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 2, 2016

By: /s/ SHANE KOVACS

Shane Kovacs

Chief Financial Officer

(Principal Financial and Accounting Officer)

Exhibit 32.1

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

In connection with the Quarterly Report on Form 10-Q of PTC Therapeutics, Inc. (the "Company") for the period ended September 30, 2016 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Stuart W. Peltz, Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that to his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: November 2, 2016

By: /s/ STUART W. PELTZ

Stuart W. Peltz
Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

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

In connection with the Quarterly Report on Form 10-Q of PTC Therapeutics, Inc. (the "Company") for the period ended September 30, 2016 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Shane Kovacs, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that to his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: November 2, 2016

By: /s/ SHANE KOVACS

Shane Kovacs
Chief Financial Officer
(Principal Financial and Accounting Officer)