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, 2018

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

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

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

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

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

As of November 1, 2018, there were 50,454,834 shares of Common Stock, $0.001 par value per share, outstanding.

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PTC Therapeutics, Inc.

FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Quarterly Report on Form 10-Q, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “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 realize the anticipated benefits of our acquisition of Agilis Biotherapeutics, Inc., or Agilis, including the possibility that the expected impact of benefits from the acquisition, including with respect to the business of Agilis and our expectations with respect to the potential achievement of development, regulatory and sales milestones and our contingent payments to the former Agilis equityholders with respect thereto, will not be realized or will not be realized within the expected time period, significant transaction costs, the integration of Agilis's operations and employees into our business, our ability to obtain marketing approval of our gene therapy for the treatment of Aromatic L-Amino Acid Decarboxylase, or AADC, deficiency, or PTC-AADC, and other product candidates we acquired from Agilis, unknown liabilities, the risk of litigation and/or regulatory actions related to the acquisition, and other business effects, including the effects of industry, market, economic, political or regulatory conditions;

- our ability to negotiate, secure and maintain adequate pricing, coverage and reimbursement terms and processes on a timely basis, or at all, with third-party payors for Emflaza™ (deflazacort) for the treatment of Duchenne muscular dystrophy, or DMD, in the United States and for Translarna™ (ataluren) for the treatment of nonsense mutation DMD, or nmDMD, in the European Economic Area, or EEA, and other countries in which we have or may obtain regulatory approval, or in which there exist significant reimbursed early access programs, or EAP programs;

- our ability to maintain our marketing authorization of Translarna for the treatment of nmDMD in the EEA (which is subject to the specific obligation to conduct and submit the results of Study 041 to the European Medicines Agency, or EMA, and annual review and renewal by the European Commission following reassessment of the benefit-risk balance of the authorization by the EMA);

- our ability to enroll, fund, and complete Study 041, a multicenter, randomized, double-blind, 18-month, placebo-controlled clinical trial of Translarna for the treatment of nmDMD followed by an 18-month open label extension, according to the protocol agreed with the EMA, and by the trial’s deadline;

- the anticipated period of market exclusivity for Emflaza for the treatment of DMD in the United States under the Orphan Drug Act of 1983, or the Orphan Drug Act, the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act and through any grant of pediatric exclusivity;

- our ability to complete the United States Food and Drug Administration, or FDA, post-marketing requirements to the marketing authorization of Emflaza or any requirements necessary to obtain any grant of pediatric exclusivity;

- our expectations with respect to our acquisition of all rights to Emflaza from Marathon Pharmaceuticals, LLC (now known as Complete Pharma Holdings, LLC), or Marathon, including with respect to our ability to realize the anticipated benefits of the acquisition (including with respect to future revenue generation and contingent payments to Marathon based on annual net sales);

- our ability to complete any dystrophin study necessary in order to resolve the matters set forth in the FDA’s denial of our appeal to the Complete Response Letter we received from the FDA in connection with our New Drug Application, or NDA, for Translarna for the treatment of nmDMD, and our ability to perform additional clinical trials, non-clinical studies or CMC assessments or analyses at significant cost;

- the timing and scope of our continued commercialization of Translarna as a treatment for nmDMD in the EEA or other territories outside of the United States;

- 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;

- our expectations and the potential financial impact and benefits related to our Collaboration and Licensing Agreement with Akcea Therapeutics, Inc., or Akcea, including with respect to the timing of regulatory approval of Tegsedi™ (inotersen) and Waylivra™ (volanesorsen) in countries in which we are licensed to commercialize them,

the potential commercialization of Tegsedi and Waylivra, and our expectations with respect to contingent payments to Akcea based on the potential achievement of certain regulatory milestones and royalty payments by us to Akcea based on our potential achievement of certain net sales thresholds;

- our estimates regarding the potential market opportunity for Translarna, Emflaza, PTC-AADC, Tegsedi, Waylivra or any other product candidate, including the size of eligible patient populations and our ability to identify such patients;
- 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 nmDMD, aniridia, and Dravet syndrome/CDKL5, each caused by nonsense mutations, as well as our studies in spinal muscular atrophy and our oncology program, including 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, Emflaza, PTC-AADC, Tegsedi and Waylivra;
- 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;
- the timing of, and our ability to obtain additional marketing authorizations for, Translarna and our other product candidates;
- the ability of Translarna, Emflaza, PTC-AADC, Tegsedi and Waylivra and our other product candidates to meet existing or future regulatory standards;
- our ability to maintain the current labeling under the marketing authorization in the EEA or expand the approved product label of Translarna for the treatment of nmDMD in non-ambulatory patients or otherwise;
- the potential receipt of revenues from future sales of Translarna, Emflaza and other product candidates, including our ability to earn a profit from sales or licenses of Translarna for the treatment of nmDMD in the countries in which we have or may obtain regulatory approval and of Emflaza for the treatment of DMD in the United States;
- the potential impact that enrollment, funding and completion of Study 041 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 and Emflaza and any other product candidate 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, Emflaza and our other product candidates that are sufficient to meet clinical trial and commercial launch requirements;
- our ability to satisfy our obligations under the terms of the credit and security agreement with MidCap Financial Trust, or MidCap Financial, as administrative agent and MidCap Financial and certain other financial institutions as lenders thereunder;
- our other regulatory submissions, including with respect to timing and outcome of regulatory review;
- our plans to pursue development of Translarna for additional indications;
- our ability to advance our earlier stage programs, including our oncology program;
- our plans to pursue research and development of other product candidates;
- whether we may pursue business development opportunities, including potential collaborations, alliances, and acquisition or licensing of assets and our ability to successfully develop or commercialize any assets to which we may gain rights pursuant to such business development opportunities;
- the potential advantages of Translarna, Emflaza, PTC-AADC, Tegsedi and Waylivra and any other product candidate;
- our intellectual property position;
- the impact of government laws and regulations;

- the impact of litigation that has or may be brought against us or of litigation that we are pursuing against others;
- 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 as well as in Part I, Item 1A. Risk Factors in our Annual Report on Form 10-K for the year ended December 31, 2017, and in Part II, Item 1A. Risk Factors in our Quarterly Reports on Form 10-Q for the periods ended March 31, 2018 and June 30, 2018, and in Exhibit 99.2 to our Current Report on Form 8-K filed on August 24, 2018, 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, our Annual Report on Form 10-K for the year ended December 31, 2017 and our Current Report on Form 8-K filed on August 24, 2018 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, 2018	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	$ 206,913	$ 111,792
Marketable securities	42,491	79,454
Trade receivables, net	42,197	40,394
Inventory, net	13,660	10,754
Prepaid expenses and other current assets	8,020	6,669
Total current assets	313,281	249,063
Fixed assets, net	8,805	8,376
Intangible assets, net	604,612	132,993
Goodwill	100,309	—
Deposits and other assets	1,620	1,221
Total assets	$ 1,028,627	$ 391,653
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable and accrued expenses	$ 102,788	$ 76,446
Current portion of long-term debt	6,667	—
Deferred revenue	2,004	3,937
Other current liabilities	3,463	1,665
Total current liabilities	114,922	82,048
Deferred revenue - long-term	11,156	7,954
Long-term debt	144,258	144,971
Contingent consideration payable	218,700	—
Deferred consideration payable	38,200	—
Deferred tax liability	115,200	—
Other long-term liabilities	101	243
Total liabilities	642,537	235,216
Stockholders' equity:		
Common stock, $0.001 par value. Authorized 125,000,000 shares; issued and outstanding 50,432,655 shares at September 30, 2018. Authorized 125,000,000 shares; issued and outstanding 41,612,395 shares at December 31, 2017	51	42
Additional paid-in capital	1,275,004	966,534
Accumulated other comprehensive income	1,628	3,969
Accumulated deficit	(890,593)	(814,108)
Total stockholders' equity	386,090	156,437
Total liabilities and stockholders' equity	$ 1,028,627	$ 391,653

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,	
	2018	2017	2018	2017
Revenues:				
Net product revenue	$ 53,021	$ 41,780	$ 177,172	$ 116,113
Collaboration and grant revenue	570	73	1,224	249
Total revenues	53,591	41,853	178,396	116,362
Operating expenses:				
Cost of product sales, excluding amortization of acquired intangible asset	3,292	1,582	8,909	2,142
Amortization of acquired intangible asset	5,793	9,716	16,815	9,952
Research and development	54,368	30,024	118,337	88,222
Selling, general and administrative	38,368	31,423	104,882	85,788
Total operating expenses	101,821	72,745	248,943	186,104
Loss from operations	(48,230)	(30,892)	(70,547)	(69,742)
Interest expense, net	(3,118)	(3,421)	(9,306)	(8,648)
Other income (expense), net	734	766	1,066	(1,373)
Loss before income tax expense	(50,614)	(33,547)	(78,787)	(79,763)
Income tax expense	(355)	(191)	(964)	(507)
Net loss attributable to common stockholders	$ (50,969)	$ (33,738)	$ (79,751)	$ (80,270)
Weighted-average shares outstanding:				
Basic and diluted (in shares)	48,096,521	41,296,740	45,310,690	38,433,749
Net loss per share—basic and diluted (in dollars per share)	$ (1.06)	$ (0.82)	$ (1.76)	$ (2.09)

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,	
	2018	2017	2018	2017
Net loss	$ (50,969)	$ (33,738)	$ (79,751)	$ (80,270)
Other comprehensive loss:				
Unrealized gain (loss) on marketable securities	33	31	(50)	—
Foreign currency translation (loss) gain	(260)	983	(2,291)	4,498
Comprehensive loss	$ (51,196)	$ (32,724)	$ (82,092)	$ (75,772)

See accompanying unaudited notes.

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

	Nine Months Ended September 30,	
	2018	**2017**
Cash flows from operating activities		
Net loss	$ (79,751)	$ (80,270)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	19,316	11,743
Change in valuation of warrant liability	3	3
Non-cash interest expense	5,563	4,999
Loss on disposal of asset	2	5
Amortization of premiums and accretion of discounts on investments, net	(354)	493
Amortization of debt issuance costs	390	308
Share-based compensation expense	24,773	24,082
Unrealized foreign currency transaction gains	(977)	(364)
Changes in operating assets and liabilities:		
Inventory	(3,252)	(3,625)
Prepaid expenses and other current assets	(1,301)	(570)
Trade receivables, net	(2,681)	(10,994)
Deposits and other assets	(385)	(485)
Accounts payable and accrued expenses	18,606	11,807
Other liabilities	1,617	807
Deferred revenue	5,933	10,710
Net cash used in operating activities	(12,498)	(31,351)
Cash flows from investing activities		
Purchases of fixed assets	(2,489)	(1,058)
Purchases of marketable securities	(28,656)	(19,467)
Sale and redemption of marketable securities	65,923	164,847
Acquisition of product rights	(3,903)	(77,163)
Business acquisition, net of cash acquired	(48,892)	—
Net cash (used in) / provided by investing activities	(18,017)	67,159
Cash flows from financing activities		
Proceeds from exercise of options	8,631	1,437
Net proceeds from public offerings	117,915	—
Proceeds from shares issued under employee stock purchase plan	1,299	1,362
Debt issuance costs related to secured term loan	—	(432)
Proceeds from issuance of secured term loan	—	40,000
Net cash provided by financing activities	127,845	42,367
Effect of exchange rate changes on cash	(2,209)	5,342
Net increase in cash and cash equivalents	95,121	83,517
Cash and cash equivalents, beginning of period	111,792	58,321
Cash and cash equivalents, end of period	$ 206,913	$ 141,838
Supplemental disclosure of cash information		
Cash paid for interest	$ 6,927	$ 5,496
Cash paid for income taxes	$ 919	$ 616
Supplemental disclosure of non-cash investing and financing activity		
Change in unrealized gain (loss) on marketable securities, net of tax	$ (50)	$ —
Acquisition of product rights and licenses	$ (4,530)	$ —

See accompanying unaudited notes.

PTC Therapeutics, Inc.
Notes to Consolidated Financial Statements (unaudited)
September 30, 2018
In thousands (except per share data unless otherwise noted)

1. The Company

PTC Therapeutics, Inc. (the "Company" or "PTC") is a science-led global biopharmaceutical company focused on the discovery, development and commercialization of clinically-differentiated medicines that provide benefits to patients with rare disorders. The Company's ability to globally commercialize products is the foundation that drives its continued investment in a robust pipeline of transformative medicines and its mission to provide access to best-in-class treatments for patients who have an unmet medical need.

The Company has two products, Translarna™ (ataluren) and Emflaza™ (deflazacort), for the treatment of Duchenne muscular dystrophy, or DMD, a rare, life threatening disorder. Translarna received marketing authorization from the European Commission in August 2014 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. In July 2018, the European Commission approved a label-extension request to the marketing authorization for Translarna in the EEA to include patients from two to up to five years of age. Emflaza is approved in the United States for the treatment of DMD in patients five years and older.

The Company has a pipeline of gene therapy product candidates, including PTC-AADC for the treatment of Aromatic L-Amino Acid Decarboxylase, or AADC, deficiency, or AADC deficiency. The Company is preparing a biologics license application, or BLA, for PTC-AADC for the treatment of AADC deficiency in the United States, which it anticipates submitting to the U.S. Food and Drug Administration, or FDA, in 2019. The Company is also preparing a marketing authorisation application, or MAA, for PTC-AADC for the treatment of AADC deficiency in the European Union, or EU, which it anticipates submitting to the European Medicines Agency, or EMA, in 2019, as well. The Company holds the rights for the commercialization of Tegsedi™ (inotersen) and Waylivra™ (volanesorsen) for the treatment of rare diseases in countries in Latin America and the Caribbean. Tegsedi has received marketing authorization in the U.S., EU and Canada for the treatment of stage 1 or stage 2 polyneuropathy in adult patients with hATTR amyloidosis. The Company plans to file a request for marketing authorization for Tegsedi with ANVISA, the Brazilian Health Regulatory Authority, in the first half of 2019. Waylivra is currently under regulatory review in EU for the treatment of familial chylomicronemia syndrome, or FCS.

The Company also has a spinal muscular atrophy (SMA) collaboration with F. Hoffman-La Roche Ltd and Hoffman-La Roche Inc., which it refers to collectively as Roche, and the Spinal Muscular Atrophy Foundation, or SMA Foundation. Currently, its collaboration has three clinical trials ongoing to evaluate the safety and effectiveness of risdiplam (RG7916, RO7034067), the lead compound in the SMA program. In addition, the Company has a pipeline of product candidates that are in early clinical and pre-clinical development. The Company's pre-clinical and discovery programs are focused on the development of new treatments for multiple therapeutic areas, including rare diseases and oncology.

The Company's marketing authorization for Translarna in the EEA is subject to annual review and renewal by the European Commission following reassessment by the EMA of the benefit-risk balance of the authorization, which the Company refers to as the annual EMA reassessment. This marketing authorization is further subject to the specific obligation to conduct and submit the results of a multi-center, randomized, double-blind, 18-month, placebo-controlled trial, followed by an 18-month open-label extension, according to an agreed protocol, in order to confirm the efficacy and safety of Translarna in the approved patient population. The final report on the trial and open-label extension is to be submitted by the Company to the EMA by the end of the third quarter of 2021. The Company refers to the trial and open-label extension together as Study 041.

The marketing authorization in the EEA was last renewed in July 2018 and is effective, unless extended, through August 5, 2019. The renewal was based on the Company's commitment to conduct Study 041 and the totality of the clinical data available from its trials and studies of Translarna for the treatment of nmDMD, including the safety and efficacy results of the Phase 2b and Phase 3 clinical trials. The primary efficacy endpoint was not achieved in either trial within the pre-specified level of statistical significance.

In June 2014, the Company initiated reimbursed early access programs, or EAP programs, for Translarna for nmDMD patients in selected territories in the EEA and recorded its first sales of Translarna in the third quarter of 2014 pursuant to an EAP program. In December 2014, the Company recorded its first commercial sales in Germany. As of September 30, 2018, Translarna was available in over 25 countries on a commercial basis or pursuant to an EAP program. The Company expects to expand its commercial activities across the EEA pursuant to the marketing authorization granted by the EMA throughout 2018 and future years, subject to continued renewal of its marketing authorization following annual EMA reassessments and successful completion of pricing and reimbursement negotiations. Concurrently, the Company plans to continue to pursue EAP programs in select countries where those mechanisms exist, both within the EEA and in other countries that will reference the marketing authorization in the EEA.

Translarna is an investigational new drug in the United States. During the first quarter of 2017, the Company filed a New Drug Application, or NDA, over protest with the United States Food and Drug Administration, (the "FDA"), for which the FDA granted a standard review. In October 2017, the Office of Drug Evaluation I of the FDA issued a complete response letter for the NDA, stating that it was unable to approve the application in its current form. In response, the Company filed a formal dispute resolution request with the Office of New Drugs of the FDA. In February 2018, the Office of New Drugs of the FDA denied PTC's appeal of the Complete Response Letter. In its response, the Office of New Drugs recommended a possible path forward for the ataluren NDA submission based on the accelerated approval pathway. This would involve a re-submission of an NDA containing the current data on effectiveness of ataluren with new data to be generated on dystrophin production in nmDMD patients' muscles. The Company intends to follow the FDA's recommendation and will collect such dystrophin data using newer technologies via procedures and methods that it is currently designing and expects to initiate such a study by the end of 2018. Additionally, should a re-submission of an NDA receive accelerated approval, the Office of New Drugs stated that Study 041, which is currently enrolling, could serve as the confirmatory post-approval trial required in connection with the accelerated approval framework.

The NDA, which seeks approval of Translarna for the treatment of nmDMD in the United States, was initially submitted by the Company in December 2015. In February 2016, following the submission, the Company received a Refuse to File letter from the FDA regarding the NDA. The FDA stated in the Refuse to File letter that the NDA was not sufficiently complete to permit a substantive review. Specifically, the Company was notified in the letter 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 the NDA did not contain adequate information regarding the abuse potential of Translarna. Additionally, the FDA stated that the Company had proposed a post-hoc adjustment of ACT DMD that eliminates data from a majority of enrolled patients. During July 2016, the Company appealed the Refuse to File decision via the formal dispute resolution process within FDA's Center for Drug Evaluation and Research; however, this appeal was denied by the FDA's Office of Drug Evaluation I in October 2016.

On April 20, 2017, the Company completed its acquisition of all rights to Emflaza, or the Transaction. Emflaza is approved in the United States for the treatment of DMD in patients five years and older. The Transaction was completed pursuant to an asset purchase agreement, dated March 15, 2017, as amended on April 20, 2017, (the "Asset Purchase Agreement"), by and between the Company and Marathon Pharmaceuticals, LLC (now known as Complete Pharma Holdings, LLC), or Marathon. The Transaction was accounted for as an asset acquisition. The assets acquired by the Company in the Transaction include intellectual property rights related to Emflaza, inventories of Emflaza, and certain contractual rights related to Emflaza. The Company assumed certain liabilities and obligations in the Transaction arising out of, or relating to, the assets acquired in the Transaction.

Upon the closing of the Transaction, the Company paid to Marathon total upfront consideration comprised of $75.0 million in cash, funded through cash on hand, and 6,683,598 shares of the Company's common stock. The number of shares of common stock issued at closing was determined by dividing $65.0 million by the volume-weighted average price per share of the Company's common stock on the Nasdaq Stock Market for the 15 trading-day period ending on the third trading day immediately preceding the closing. Marathon is entitled to receive contingent payments from the Company based on annual net sales of Emflaza, up to a specified aggregate maximum amount over the expected commercial life of the asset, and a single $50.0 million sales-based milestone, in each case subject to the terms and conditions of the Asset Purchase Agreement.

On August 23, 2018, the Company completed its acquisition of Agilis Biotherapeutics, Inc., or Agilis, pursuant to an Agreement and Plan of Merger, dated as of July 19, 2018 (the "Merger Agreement"), by and among the Company, Agility Merger Sub, Inc., a Delaware corporation and the Company's wholly owned, indirect subsidiary, Agilis and, solely in its capacity as the representative, agent and attorney-in-fact of the equityholders of Agilis, Shareholder Representative Services LLC, (the "Merger").

Upon the closing of the Merger, the Company paid to Agilis equityholders total upfront consideration comprised of $49.2 million in cash and 3,500,907 shares of the Company's common stock (the "Closing Stock Consideration"). The Closing Stock Consideration was determined by dividing $150.0 million by the volume-weighted average price per share of the Company's common stock on the Nasdaq Global Select Market for the 10 consecutive trading-day period ending on the second trading-day immediately preceding the closing of the Merger. Agilis equityholders may become entitled to receive contingent payments from the Company based on the achievement of certain development, regulatory and net sales milestones as well as based upon a percentage of net sales of certain products. Under the Merger Agreement, the Company is required to pay $40.0 million of the development milestone payments no later than the second anniversary of the closing of the Merger, regardless of whether the applicable milestones have been achieved.

As of September 30, 2018, the Company had an accumulated deficit of approximately $890.6 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 10), public offerings of common stock in February 2014, October 2014 and April 2018, 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. Since 2014, the Company has also relied on revenue generated from net sales of Translarna for the treatment of nmDMD in territories outside of the United States, and in May 2017, the Company began

to recognize revenue generated from net sales of Emflaza for the treatment of DMD in the United States. The Company expects that the cash flows from the sales of its products, together with the Company's cash, cash equivalents and marketable securities, will be sufficient to fund its operations for at least the next twelve months.

2. Summary of significant accounting policies

The Company's complete listing of significant accounting policies is set forth in Note 2 of the notes to the Company's audited financial statements as of December 31, 2017 included in the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission (the "SEC") on March 6, 2018 (the "2017 Form 10-K"). Additional significant accounting policies adopted during the nine month period ended September 30, 2018 are discussed in further detail below.

Basis of presentation

The accompanying financial information as of September 30, 2018 and for the three and nine months ended September 30, 2018 and 2017 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, 2017 and notes thereto included in the 2017 Form 10-K.

In the opinion of management, the unaudited financial information as of September 30, 2018 and for the three and nine months ended September 30, 2018 and 2017 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, 2018 are not necessarily indicative of the results to be expected for the year ended December 31, 2018 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, inventory, acquired intangible assets, fair value of the contingent consideration, 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.

Inventory and cost of product sales

Inventory

Inventories are stated at the lower of cost and net realizable value with cost determined on a first-in, first-out basis by product. The Company capitalizes inventory costs associated with products following regulatory approval when future commercialization is considered probable and the future economic benefit is expected to be realized. Translarna and Emflaza product which may be used in clinical development programs are included in inventory and charged to research and development expense when the product enters the research and development process and no longer can be used for commercial purposes. Inventory used for marketing efforts are charged to selling, general and administrative expense.

The following table summarizes the components of the Company's inventory for the periods indicated:

	September 30, 2018	December 31, 2017
Raw materials	$ 399	$ 452
Work in progress	5,997	3,912
Finished goods	7,264	6,390
Total inventory	$ 13,660	$ 10,754

The Company periodically reviews its inventories for excess amounts or obsolescence and writes down obsolete or otherwise unmarketable inventory to its estimated net realizable value. The Company recorded a $1.6 million inventory write down for the three month period ended September 30, 2018 primarily related to inventory labeling changes. Additionally, though the Company's product is subject to strict quality control and monitoring which it performs throughout the manufacturing processes, certain

batches or units of product may not meet quality specifications resulting in a charge to cost of product sales. For the three and nine month periods ended September 30, 2018, these amounts were immaterial.

Cost of product sales

Cost of product sales consists of the cost of inventory sold, manufacturing and supply chain costs, storage costs, amortization of the acquired intangible asset and royalty payments associated with net product sales.

Revenue recognition

In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2014-9, "Revenue from Contracts with Customers (Topic 606)". ASU No. 2014-9 eliminated transaction- and industry-specific revenue recognition guidance under FASB Accounting Standards Codification ("ASC") Subtopic 605-15, Revenue Recognition-Products (Topic 605) and replaced it with a principle-based approach for determining revenue recognition. ASC Topic 606 requires entities to 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. On January 1, 2018, the Company adopted ASC Topic 606 using the modified retrospective approach, a practical expedient permitted under Topic 606, and applied this approach only to contracts that were not completed as of January 1, 2018. The Company calculated a one-time transition adjustment of $3.3 million, which was recorded on January 1, 2018 to the opening balance of accumulated deficit, related to the product sales of Emflaza. The ASC 606 transition adjustment recorded for Emflaza resulted in sales being recognized earlier than under Topic 605, as the deferred revenue recognition model (sell-through) is not applicable under Topic 606. The one-time adjustment consisted of $3.9 million in deferred revenue offset by $0.6 million of variable consideration. The information presented for the periods prior to January 1, 2018 has not been adjusted and is reported under Topic 605.

Periods prior to January 1, 2018

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

Prior to the second quarter of 2017, the Company's net product sales consisted of sales of Translarna for the treatment of nmDMD in territories outside of the U.S. 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 the Company's third-party partner distributors. Revenue is recognized when risk of ownership has transferred. 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.

In May 2017, the Company began the commercialization of Emflaza in the U.S. The Company recorded product revenue related to the sales of Emflaza in the U.S. in accordance with ASC 605-15, when persuasive evidence of an arrangement exists, delivery has occurred and title of the product and associated risk of loss has passed to the customer, the price is fixed or determinable and collection from the customer has been reasonably assured. Due to the early stage of the product launch, the Company determined that it was not able to reliably make certain estimates, including returns, necessary to recognize product revenue upon shipment to distributors. As a result, the Company recorded net product revenue for Emflaza using a deferred revenue recognition model (sell-through). Under the deferred revenue model, the Company does not recognize revenue until Emflaza is shipped to the specialty pharmacy.

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 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 its 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.

Periods commencing January 1, 2018

The Company's net product revenue consists of sales of Translarna in territories outside of the U.S. and sales of Emflaza in the U.S., both for the treatment of DMD.

Net product revenue

The Company recognizes revenue when its performance obligations with its customers have been satisfied. The Company’s performance obligations are to provide Translarna or Emflaza based on customer orders from distributors, hospitals, specialty pharmacies or retail pharmacies. The performance obligations are satisfied at a point in time when the Company’s customer obtains control of either Translarna or Emflaza, which is typically upon delivery. The Company invoices its customers after the products have been delivered and invoice payments are generally due within 30 to 90 days of invoice date. The Company determines the transaction price based on fixed consideration in its contractual agreements. Contract liabilities arise in certain circumstances when consideration is due for goods the Company has yet to provide. As the Company has identified only one distinct performance obligation, the transaction price is allocated entirely to either product sales of Translarna or Emflaza. In determining the transaction price, a significant financing component does not exist since the timing from when the Company delivers product to when the customers pay for the product is typically less than one year. Customers in certain countries pay in advance of product delivery. In those instances, payment and delivery typically occur in the same month.

The Company records product sales net of any variable consideration, which includes discounts, allowances, rebates and distribution fees. The Company uses the expected value or most likely amount method when estimating its variable consideration, unless discount or rebate terms are specified within contracts. Historically, returns of Translarna and Emflaza are immaterial to the financial statements. The identified variable consideration is recorded as a reduction of revenue at the time revenues from product sales are recognized. These estimates for variable consideration are adjusted to reflect known changes in factors and may impact such estimates in the quarter those changes are known. Revenue recognized does not include amounts of variable consideration that are constrained.

In relation to customer contracts, the Company incurs costs to fulfill a contract but does not incur costs to obtain a contract. These costs to fulfill a contract do not meet the criteria for capitalization and are expensed as incurred.

Upon adoption of ASC Topic 606 on January 1, 2018, the Company elected the following practical expedients:

- Portfolio Approach - the Company applied the Portfolio Approach to contract reviews within its identified revenue streams that have similar characteristics and the Company believes this approach would not differ materially than if applying ASC Topic 606 to each individual contract.

- Significant Financing Component - the Company expects the period between when it transfers a promised good to a customer and when the customer pays for the good or service to be one year or less.

- Immaterial Performance Obligations - the Company disregards promises deemed to be immaterial in the context of the contract.

- Shipping and Handling Activities - the Company considers any shipping and handling costs that are incurred after the customer has obtained control of the product as a cost to fulfill a promise.

Shipping and handling costs associated with finished goods delivered to customers are recorded as a selling expense.

Collaboration 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.

At the inception of a collaboration arrangement, the Company needs to first evaluate if the arrangement meets the criteria in ASC Topic 808 “Collaborative Arrangements” to then determine if ASC Topic 606 is applicable by considering whether the collaborator meets the definition of a customer. If the criteria are met, the Company assesses the promises in the arrangement to identify distinct performance obligations.

For licenses of intellectual property, the Company assesses, at contract inception, whether the intellectual property is distinct from other performance obligations identified in the arrangement. If the licensing of intellectual property is determined to be distinct, revenue is recognized for nonrefundable, upfront license fees when the license is transferred to the customer and the customer can use and benefit from the license. If the licensing of intellectual property is determined not to be distinct, then the license will be bundled with other promises in the arrangement into one distinct performance obligation. The Company needs to determine if the bundled performance obligation is satisfied over time or at a point in time. If the Company concludes that the nonrefundable, upfront license fees will be recognized over time, the Company will need to assess the appropriate method of measuring proportional performance.

For milestone payments, the Company assesses, at contract inception, whether the development or sales-based milestones are considered probable of being achieved. If it is probable that a significant revenue reversal will occur, the Company will not record revenue until the uncertainty has been resolved. Milestone payments that are contingent upon regulatory approval are not considered probable of being achieved until the applicable regulatory approvals or other external conditions are obtained as such conditions are not within the Company's control. If it is probable that a significant revenue reversal will not occur, the Company will estimate the milestone payments using the most likely amount method. The Company will re-assess the development and sales-based milestones each reporting period to determine the probability of achievement.

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 $0.6 million as of September 30, 2018 and $0.8 million as of December 31, 2017.

Indefinite-lived intangible assets

Indefinite-lived intangible assets consist of in-process research and development (IPR&D). IPR&D acquired directly in a transaction other than a business combination is capitalized if the projects will be further developed or have an alternative future use; otherwise they are expensed. The fair values of IPR&D projects acquired in business combinations are capitalized. Several methods may be used to determine the estimated fair value of the IPR&D acquired in a business combination. The Company utilizes the "income method”, and uses estimated future net cash flows that are derived from projected sales revenues and estimated costs. These projections are based on factors such as relevant market size, patent protection, and expected pricing and industry trends. The estimated future net cash flows are then discounted to the present value using an appropriate discount rate. These assets are treated as indefinite-lived intangible assets until completion or abandonment of the projects, at which time the assets are amortized over the remaining useful life or written off, as appropriate. IPR&D intangible assets that are determined to have had a drop in their fair value are adjusted downward and an impairment is recognized in the statement of operations. These assets are tested at least annually or sooner when a triggering event occurs that could indicate a potential impairment.

Goodwill

Goodwill represents the amount of consideration paid in excess of the fair value of net assets acquired as a result of the Company’s business acquisitions accounted for using the acquisition method of accounting. Goodwill is not amortized and is subject to impairment testing on an annual basis or when a triggering event occurs that may indicate the carrying value of the goodwill is impaired.

Income Taxes

On December 22, 2017, the U.S. government enacted the 2017 Tax Cuts and Jobs Act (the 2017 Tax Act), which significantly revises U.S. tax law by, among other provisions, lowering the U.S. federal statutory income tax rate to 21%, imposing a mandatory one-time transition tax on previously deferred foreign earnings, and eliminating or reducing certain income tax deductions. The Global Intangible Low-tax Income (GILTI) provisions of the 2017 Tax Act require the Company to include in its U.S. income tax return foreign subsidiary earnings in excess of an allowable return on the foreign subsidiary's tangible assets. The Company has elected to account for GILTI tax in the period in which it is incurred, and therefore has not provided any deferred tax impacts of GILTI in its consolidated financial statements for the period ended September 30, 2018.

ASC 740, Income Taxes requires the effects of changes in tax laws to be recognized in the period in which the legislation is enacted. However, due to the complexity and significance of the 2017 Tax Act's provisions, the SEC issued SAB 118, which allows companies to record the tax effects of the 2017 Tax Act on a provisional basis based on a reasonable estimate, and then, if necessary, subsequently adjust such amounts during a limited measurement period as more information becomes available. The measurement period ends when a company has obtained, prepared, and analyzed the information necessary to finalize its accounting, but cannot extend beyond one year from enactment. The 2017 Tax Act does not have a material impact on the Company's financial statements since its deferred temporary differences are fully offset by a valuation allowance and the Company does not have any significant off shore earnings from which to record the mandatory transition tax. However, given the significant complexity of the 2017 Tax Act, anticipated guidance from the U.S. Treasury about implementing the 2017 Tax Act, and the potential for additional guidance from the SEC or the FASB related to the 2017 Tax Act, these estimates may be adjusted during the measurement period. The Company continues to analyze the changes in certain income tax deductions, assess calculations of earnings and profits in certain foreign subsidiaries, including if those earnings which are held in cash or other assets and gather additional data to compute the full impacts on the Company's deferred and current tax assets and liabilities.

The Company recorded a deferred tax liability in conjunction with the Merger, further discussed in Note 3, of $115.2 million related to the tax basis difference in the IPR&D indefinite-lived intangibles acquired. The Company's policy is to record a deferred tax liability related to acquired IPR&D which may eventually be realized either upon amortization of the asset when the research is completed and a product is successfully launched or the write-off of the asset if it is abandoned or unsuccessful.

Recently issued accounting standards

In February 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("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, as well as the impact on internal control over financial reporting.

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 January 2017, the FASB issued ASU 2017-04, "Simplifying the Test for Goodwill Impairment". This standard simplifies the accounting for goodwill impairment by requiring impairment charges to be based on the first step in today's two-step impairment test under ASC 350. Therefore, entities will record an impairment charge based on the excess of a reporting unit's carrying amount over its fair value. The guidance is effective for annual and interim impairment tests performed in periods beginning after December 15, 2019 for public business entities that meet the definition of an SEC filer, December 15, 2020 for public business entities that are not SEC filers, and December 15, 2021 for all other entities. Early adoption is permitted for all entities for annual and interim goodwill impairment testing dates on or after January 1, 2017. The guidance should be applied on a prospective basis. The Company expects to adopt this guidance when effective and is currently assessing what effect the adoption of ASU No. 2017-04 will have on its consolidated financial statements and accompanying notes.

In February 2018, the FASB issued ASU 2018-02, "Income Statement — Reporting Comprehensive Income (Topic 220): Reclassification of Certain Tax Effects from Accumulated Other Comprehensive Income". This standard permits the reclassification of tax effects stranded in other comprehensive income as a result of tax reform to retained earnings related to the change in federal tax rate in addition to other stranded effects that relate to the Tax Cuts and Job Act ("the Act") but do not directly relate to the

change in the federal rate. ASU 2018-02 is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years with early adoption permitted for periods for which financial statements have not yet been issued or made available for issuance. The Company expects to adopt this guidance when effective and is currently assessing what effect the adoption of ASU No. 2018-02 will have on its consolidated financial statements and accompanying notes.

In June 2018, the FASB issued ASU 2018-07, "Compensation — Stock Compensation (Topic 718), Improvements to Nonemployee Share-Based Payment Accounting". This standard expands the scope of ASC 718 to include share-based payments granted to nonemployees in exchange for goods or services used or consumed in the entity's own operations and supersedes the guidance in ASC 505-50. The ASU retains the existing cost attribution guidance, which requires entities to recognize compensation cost for nonemployee awards in the same period and in the same manner they would if they paid cash for the goods or services, but it moves the guidance to ASC 718. ASU 2018-07 is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years with early adoption permitted for periods for which financial statements have not yet been issued or made available for issuance. The Company expects to adopt this guidance when effective and is currently assessing what effect the adoption of ASU No. 2018-07 will have on its consolidated financial statements and accompanying notes.

In August 2018, the FASB issued ASU 2018-13, "Fair Value Measurement (Topic 820), Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement". This standard eliminates certain disclosure requirements for fair value measurements for all entities, requires public entities to disclose certain new information and modifies some disclosure requirements. The new guidance is effective for all entities for fiscal years beginning after December 15, 2019 and for interim periods within those fiscal years. An entity is permitted to early adopt either the entire standard or only the provisions that eliminate or modify requirements. Entities can elect to early adopt in interim periods, including periods for which they have not yet issued financial statements or made their financial statements available for issuance. The Company expects to adopt this guidance when effective and is currently assessing what effect the adoption of ASU No. 2018-13 will have on its consolidated financial statements and accompanying notes.

In August 2018, the FASB issued ASU 2018-15,"Intangibles - Goodwill and Other - Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract". ASU 2018-15 requires a customer in a cloud computing arrangement that is a service contract to follow the internal-use software guidance in Accounting Standards Codification 350-40 to determine which implementation costs to defer and recognize as an asset. For public business entities, the guidance is effective for annual periods, and interim periods within those annual periods, beginning after December 15, 2019. For all other entities, it is effective for annual periods beginning after December 15, 2020 and interim periods in annual periods beginning after December 15, 2021. Early adoption is permitted, including adoption in any interim period for all entities. The Company expects to adopt this guidance when effective and is currently assessing what effect the adoption of ASU No. 2018-13 will have on its consolidated financial statements and accompanying notes.

Impact of recently adopted accounting pronouncements

In May 2014, the FASB issued ASU No. 2014-09, "Revenue from Contracts with Customers (Topic 606)". ASU No. 2014-09 eliminated transaction- and industry-specific revenue recognition guidance under FASB Accounting Standards Codification ("ASC") Subtopic 605-15, Revenue Recognition-Products and replaced it with a principle-based approach for determining revenue recognition. ASC Topic 606 requires entities to 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. On January 1, 2018, the Company adopted ASC Topic 606 using the modified retrospective approach and applied this approach only to contracts that were not completed as of January 1, 2018. The Company calculated a one-time transition adjustment of $3.3 million, which was recorded on January 1, 2018 to deferred revenue and accumulated deficit, related to the product sales of Emflaza. The information presented for the periods prior to January 1, 2018 has not been restated and is reported under ASC Topic 605.

In January 2016, the FASB issued ASU No. 2016-01, "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. The Company adopted ASU 2016-01 during the three months ended March 31, 2018. In March 2018, the FASB issued ASU 2018-04, "Investments - Debt Securities (Topic 320) and Regulated Operations (Topic 980): Amendments to SEC Paragraphs Pursuant to the SEC Staff Accounting Bulletin ("SAB") No. 117 and SEC Release No. 33-9273 (SEC Update)". This standard supersedes SEC paragraphs in ASC 320, Investments-Debt Securities, as a result of the issuance of SAB 117 and also updates the Codification for a 2011 SEC release and is effective when a registrant adopts ASU 2016-01, which in the case of the Company was during the three months ended March 31, 2018. The adoption of these standards did not have a material impact on the Company's financial position or results of operations for the period ended and as of September 30, 2018.

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 Company adopted ASU 2016-15 during the three months ended March 31, 2018. The adoption of this standard did not have a material impact on the Company’s financial position or results of operations for the period ended and as of September 30, 2018.

In November 2016, the FASB issued ASU No. 2016-18, “Statement of Cash Flows (Topic 230): Restricted Cash”. This standard requires entities to show the changes in the total of cash, cash equivalents, restricted cash and restricted cash equivalents in the statement of cash flows and no longer present transfers between cash and cash equivalents and restricted cash and restricted cash equivalents in the statement of cash flows. The Company adopted ASU 2016-18 during the three months ended March 31, 2018. The adoption of this standard did not have a material impact on the Company’s financial position or results of operations for the period ended and as of September 30, 2018.

In May 2017, the FASB issued ASU No. 2017-09, "Stock Compensation (Topic 718): Scope of Modification Accounting". This standard clarifies when changes to the terms or conditions of a share-based payment award must be accounted for as a modification, with entities applying the modification accounting guidance if the value, vesting conditions or classification of the award changes. In addition to all disclosures about modifications that are required under the current guidance, entities will be also required to disclose that compensation expense has not changed if applicable. The Company adopted ASU 2017-09 during the three months ended March 31, 2018. The adoption of this standard did not have a material impact on the Company’s financial position or results of operations for the period ended and as of September 30, 2018.

3. Business combination

On August 23, 2018, the Company completed its acquisition of Agilis pursuant to the Merger Agreement. Agilis was a privately-held biotechnology company advancing an innovative gene therapy platform for rare monogenic diseases that affect the central nervous system. Upon completion of the Merger, the Company acquired Agilis's lead product candidate, PTC-AADC, for the treatment of AADC deficiency, as well as three other gene therapies that were part of the Agilis platform.

Upon the closing of the Merger, the Company paid to Agilis equityholders total upfront consideration comprised of $49.2 million in cash and 3,500,907 shares of the Company’s common stock (the “Closing Stock Consideration”). The Closing Stock Consideration was determined by dividing $150.0 million by the volume-weighted average price per share of the Company’s common stock on the Nasdaq Global Select Market for the 10 consecutive trading-day period ending on the second trading-day immediately preceding the closing of the Merger. The fair value of the stock on the acquisition date was determined to be $155.9 million.

Pursuant to the Merger Agreement, Agilis equityholders may become entitled to receive contingent consideration payments from the Company based on (i) the achievement of certain development milestones up to an aggregate maximum amount of $60.0 million, (ii) the achievement of certain regulatory approval milestones together with a milestone payment following the receipt of a priority review voucher up to an aggregate maximum amount of $535.0 million, (iii) the achievement of certain net sales milestones up to an aggregate maximum amount of $150.0 million, and (iv) a percentage of annual net sales for Friedreich Ataxia and Angelman Syndrome during specified terms, ranging from 2-6%. The fair value of the contingent consideration payments at the acquisition date was estimated to be $218.7 million and was determined by applying a probability adjusted, discounted cash flow approach based on development timelines from the acquired product candidates and estimated future sales. Under the Merger Agreement, the Company is required to pay $40.0 million of the development milestone payments mentioned above no later than the second anniversary of the closing of the Merger, regardless of whether the applicable milestones have been achieved. The fair value of the deferred consideration payments at the closing date was estimated to be $38.2 million. Refer to Footnote 4 for further fair value considerations.

The Company evaluated the acquisition of Agilis under ASU No. 2017-01, *Business Combinations: Clarifying the Definition of a Business*. Because the business contained both inputs and processes necessary to manage products and provide economic benefits directly to its owners and substantially all the value of the acquisition did not relate to a similar group of assets, it was determined that the acquisition represents a business combination. Therefore, the transaction has been accounted for using the acquisition method of accounting. Under the acquisition method of accounting, the total purchase price of the acquisition is allocated to the net tangible and identifiable intangible assets acquired and liabilities assumed based on their fair values as of the date of acquisition.

The fair value of consideration totaled approximately $462.0 million summarized as follows:

		As of August 23, 2018
Cash consideration	$	49,221
Fair value of PTC common stock issued		155,860
Estimated fair value of deferred consideration payable		38,200
Estimated fair value of contingent consideration payable		218,700
Total consideration	$	461,981

The Company recorded the assets acquired and liabilities assumed as of the date of acquisition based on the information available at that time. As the Company finalizes the fair values of the assets acquired and liabilities assumed, purchase price adjustments may be recorded during the measurement period and such adjustments could be material. The Company will reflect measurement period adjustments, if any, in the period in which the adjustments are recognized. No adjustments have been made as of the acquisition date of August 23, 2018 through the period ended September 30, 2018.

The following table presents the preliminary allocation of the purchase price to the estimated fair values of the assets acquired and liabilities assumed as of the acquisition date of August 23, 2018, and through the period ended September 30, 2018:

		Preliminary Allocation as of the acquisition date and as at September 30, 2018
Cash and cash equivalents	$	328
Prepaid expenses and other current assets		181
Fixed assets		153
Other assets		38
Intangible assets - in process research and development (“IPRD”)		480,000
Accounts payable and accrued expenses		(3,828)
Deferred tax liability		(115,200)
Fair value of net assets acquired	$	361,672
Goodwill		100,309
Total purchase price	$	461,981

The Company incurred approximately $1.5 million in acquisition related expenses as of September 30, 2018, which were included in selling, general and administrative expenses in the consolidated statement of operations. The results of Agilis’s operations have been included in the consolidated statements of operations beginning on the acquisition date of August 23, 2018.

The fair value of the IPR&D will be capitalized as of the acquisition date and subsequently accounted for as indefinite-lived intangible assets until disposition of the assets or completion or abandonment of the associated research and development efforts. Accordingly, during the development period after the completion of the acquisition, these assets will not be amortized into earnings; rather, these assets will be subject to periodic impairment testing. Upon successful completion of the development efforts, the useful lives of the IPR&D assets will be determined and the assets will be considered definite-lived intangible assets and amortized over their expected useful lives.

The goodwill recorded is the excess of the purchase price of the net assets acquired net of any deferred tax adjustments. The Company currently has a deferred tax liability for the indefinite lived IPR&D intangible assets, which have no tax basis and, therefore, will not result in a future tax deduction. The goodwill is not deductible for income tax purposes.

The net loss of Agilis included in the consolidated statement of operations for the period August 23, 2018 through September 30, 2018 was $1.9 million.

Pro-Forma Financial Information Associated with the Agilis Acquisition (Unaudited)

The following table summarizes certain supplemental pro forma financial information for the three and nine-month periods ended September 30, 2018 and 2017 as if the Merger had occurred as of January 1, 2017. The unaudited pro-forma financial information

for the three month and nine month periods ended September 30, 2018 reflects adjustments of $0.8 million and $1.5 million, respectively, related to acquisition fees that are non-recurring in nature. There were no adjustments related to the three and nine month periods ended September 30, 2017.

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2018	2017	2018	2017
Revenues	$ 53,591	$ 41,853	$ 178,396	$ 116,362
Net loss attributable to common stockholders	(52,458)	(41,606)	(89,976)	(90,795)

Bridge Loan

In connection with the Merger Agreement, on July 19, 2018, the Company also entered into a Bridge Loan and Security Agreement, or the Bridge Loan Agreement, by and among the Company, Agilis and certain of Agilis's domestic subsidiaries, as guarantors. Under the Bridge Loan Agreement, the Company made a term loan advance to Agilis on July 23, 2018 in an original principal amount of $10.0 million. In connection with the closing of the Merger, the original principal amount of $10.0 million plus all accrued and unpaid interest thereon was credited against the cash portion of the upfront consideration paid by the Company pursuant to the terms of the Merger Agreement in satisfaction of Agilis's outstanding payment obligations under the Bridge Loan Agreement, and the Company will have no further obligation to extend any further loan amounts under the Bridge Loan Agreement.

4. Fair value of financial instruments and marketable securities

The Company follows the fair value measurement rules, which provide 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 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, 2018 and December 31, 2017:

	September 30, 2018			
	Total	Quoted prices in active markets for identical assets (level 1)	Significant other observable inputs (level 2)	Significant unobservable inputs (level 3)
Marketable securities	$ 42,491	$ —	$ 42,491	$ —
Warrant liability	$ 4	$ —	$ —	$ 4
Stock appreciation rights liability	$ 3,463	$ —	$ —	$ 3,463
Deferred consideration payable	$ 38,200	$ —	$ 38,200	$ —
Contingent consideration payable	$ 218,700	$ —	$ —	$ 218,700

	December 31, 2017			
	Total	Quoted prices in active markets for identical assets (level 1)	Significant other observable inputs (level 2)	Significant unobservable inputs (level 3)
Marketable securities	$ 79,454	$ —	$ 79,454	$ —
Warrant Liability	$ 1	$ —	$ —	$ 1
Stock appreciation rights liability	$ 1,665	$ —	$ —	$ 1,665
Deferred consideration payable	$ —	$ —	$ —	$ —
Contingent consideration payable	$ —	$ —	$ —	$ —

No transfers of assets between Level 1 and Level 2 of the fair value measurement hierarchy occurred during the periods ended September 30, 2018 and December 31, 2017.

The following is a summary of marketable securities accounted for as available-for-sale securities at September 30, 2018 and December 31, 2017:

	September 30, 2018			
	Amortized Cost	Gross Unrealized		Fair Value
		Gains	Losses	
Commercial paper	$ 18,441	$ —	$ (6)	$ 18,435
Corporate debt securities	24,078	2	(24)	24,056
	$ 42,519	$ 2	$ (30)	$ 42,491

	December 31, 2017			
	Amortized Cost	Gross Unrealized		Fair Value
		Gains	Losses	
Commercial paper	$ 13,775	$ 52	$ —	$ 13,827
Corporate debt securities	65,657	—	(30)	65,627
	$ 79,432	$ 52	$ (30)	$ 79,454

At September 30, 2018 and December 31, 2017, 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, 2018 and December 31, 2017, the Company did not have any realized gains/losses from the sale of marketable securities.

The unrealized losses and fair values of available-for-sale securities that have been in an unrealized loss position for a period of less than and greater than 12 months as of September 30, 2018 are as follows:

	September 30, 2018					
	Securities in an unrealized loss position less than 12 months		Securities in an unrealized loss position greater than 12 months		Total	
	Unrealized losses	Fair Value	Unrealized losses	Fair Value	Unrealized losses	Fair Value
Commercial paper	$ (6)	$ 18,435	$ —	$ —	$ (6)	$ 18,435
Corporate debt securities	(24)	18,067	—	—	(24)	18,067
	$ (30)	$ 36,502	$ —	$ —	$ (30)	$ 36,502

The unrealized losses and fair values of available-for-sale securities that have been in an unrealized loss position for a period of less than and greater than 12 months as of December 31, 2017 are as follows:

	December 31, 2017					
	Securities in an unrealized loss position less than 12 months		Securities in an unrealized loss position greater than 12 months		Total	
	Unrealized losses	Fair Value	Unrealized losses	Fair Value	Unrealized losses	Fair Value
Corporate debt securities	$ (28)	$ 59,108	$ (2)	$ 6,519	$ (30)	$ 65,627

Marketable securities on the balance sheet at September 30, 2018 and December 31, 2017 mature as follows:

	September 30, 2018	
	Less Than 12 Months	More Than 12 Months
Commercial paper	$ 18,435	$ —
Corporate debt securities	24,056	—
Total Marketable securities	$ 42,491	$ —

	December 31, 2017	
	Less Than 12 Months	More Than 12 Months
Commercial paper	$ 13,827	$ —
Corporate debt securities	55,550	10,077
Total Marketable securities	$ 69,377	$ 10,077

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

Convertible 3.0% senior notes

In August 2015, the Company issued $150.0 million of 3.0% convertible senior notes due August 15, 2022 (the “Convertible Notes”). Interest is payable semi-annually on February 15 and August 15 of each year, beginning on February 15, 2016. The Company separately accounted for the liability and equity components of the Convertible Notes by allocating the proceeds between the liability component and equity component, as further discussed in Note 10. The fair value of the Convertible Notes, which differs from their carrying values, is influenced by interest rates, the Company’s stock price and stock price volatility and is determined by prices for the Convertible Notes observed in market trading which are Level 2 inputs. The estimated fair value of the Convertible Notes at September 30, 2018 and December 31, 2017 was $172.9 million and $115.7 million, respectively.

The carrying amounts reported in the consolidated balance sheets for cash and cash equivalents, accounts receivable, accounts payable and borrowings under the credit and security agreement with MidCap Financial Trust and other financial institutions (as further discussed in Note 10) approximate fair value because of the immediate or short-term maturity of these financial instruments. The carrying amounts for the credit and security agreement approximate fair value based on market activity for other debt instruments with similar characteristics and comparable risk.

Deferred consideration payable

Pursuant to the Merger Agreement with Agilis, the Company is required to pay $40.0 million of development milestone payments no later than the second anniversary of the closing of the Merger, regardless of whether the applicable milestones have been achieved. The fair value of the deferred consideration payments at the acquisition date was estimated to be $38.2 million based on calculating the present value utilizing discount rates for BBB rated bonds maturing in the years of expected payments.

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 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 contingent consideration payable is fair valued each reporting period with the change in fair value recorded as a gain or loss in the consolidated statements of operations. The Company estimates the fair value of its contingent consideration using a probability weighted discounted cash flow valuation approach based on development timelines and the estimated future sales expected from the Agilis platform.

The table presented below is a summary of changes in the fair value of the Company's Level 3 valuations for the warrant liability, the SARs liability, and the contingent consideration payable for the period ended September 30, 2018:

	Level 3 liabilities		
	Warrants	SARs	Contingent consideration payable
Beginning balance as of December 31, 2017	$ 1	$ 1,665	$ —
Additions	—	—	218,700
Change in fair value	3	3,789	—
Payments	—	(1,991)	$ —
Ending balance as of September 30, 2018	$ 4	$ 3,463	$ 218,700

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, 2018 include (i) volatility (51%-54%), (ii) risk free interest rate (2.59%-2.59%), (iii) strike price ($128.00-$2,520.00), (iv) fair value of common stock ($47.00), and (v) expected life (0.8—1.0 years). The significant assumptions used in preparing the option pricing model for valuing the Company's warrants as of December 31, 2017 include (i) volatility (69%-69%), (ii) risk free interest rate (1.89%—1.89%), (iii) strike price ($128.00—$2,520.00), (iv) fair value of common stock ($16.68), and (v) expected life (1.6—1.7 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, 2018 include (i) volatility (45%—54%), (ii) risk free interest rate (2.19%—2.70%), (iii) strike price ($6.76-$30.86), (iv) fair value of common stock ($47.00), and (v) expected life (0.3—1.3 years). The significant assumptions used in preparing the option pricing model for valuing the Company's SARs as of December 31, 2017 include (i) volatility (31%-70%), (ii) risk free interest rate (1.28%—1.89%), (iii) strike price ($6.76—$30.86), (iv) fair value of common stock ($16.68), and (v) expected life (0.0—2.0 years).

Fair value of the contingent consideration liability is estimated using a probability weighted discounted cash flow approach. Some of the more significant assumptions made in the valuation include (i) the estimated revenue forecasts, (ii) probabilities of success, and (iii) discount periods and rate. The probability of achievement of regulatory and sales milestones ranged from 25% to 89%. The achievement of certain development milestones ranged from zero to an aggregate maximum amount of $20.0 million, the achievement of certain regulatory approval milestones together with a milestone payment following the receipt of a priority review voucher ranged from zero up to an aggregate maximum amount of $535.0 million, the achievement of certain net sales milestones ranged from zero up to an aggregate maximum amount of $150.0 million, and a percentage of annual net sales for Friedreich Ataxia and Angelman Syndrome during specified terms, ranging from 2-6%, in periods which sales occur. The $20.0 million

development milestones mentioned above do not include $40.0 million in development milestone payments that the Company is required to pay no later than the second anniversary of the closing of the Merger, regardless of whether the applicable milestones have been achieved. Such $40 million development milestones have been recorded as deferred consideration payable on the consolidated balance sheets at its estimated fair value, which was estimated to be $38.2 million.

The contingent consideration is classified as a Level 3 liability as its valuation requires substantial judgment and estimation of factors that are not currently observable in the market. If different assumptions were used for the various inputs to the valuation approach, including but not limited to, assumptions involving probability adjusted sales estimates for the Agilis platform and estimated discount rates, the estimated fair value could be significantly higher or lower than the fair value determined.

5. 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, 2018:

	Unrealized Gains/(Losses) On Marketable Securities, net of tax	Foreign Currency Translation	Total Accumulated Other Comprehensive Items
Balance at June 30, 2018	$ (61)	$ 1,916	$ 1,855
Other comprehensive income (loss) before reclassifications	33	(260)	(227)
Amounts reclassified from other comprehensive items	—	—	—
Other comprehensive income (loss)	33	(260)	(227)
Balance at September 30, 2018	$ (28)	$ 1,656	$ 1,628

	Unrealized Gains/(Losses) On Marketable Securities, net of tax	Foreign Currency Translation	Total Accumulated Other Comprehensive Items
Balance at December 31, 2017	$ 22	$ 3,947	$ 3,969
Other comprehensive loss before reclassifications	(50)	(2,291)	(2,341)
Amounts reclassified from other comprehensive items	—	—	—
Other comprehensive loss	(50)	(2,291)	(2,341)
Balance at September 30, 2018	$ (28)	$ 1,656	$ 1,628

6. Accounts payable and accrued expenses

Accounts payable and accrued expenses at September 30, 2018 and December 31, 2017 consist of the following:

	September 30, 2018	December 31, 2017
Employee compensation, benefits, and related accruals	$ 18,003	$ 17,711
Consulting and contracted research	8,111	5,137
Professional fees	3,541	2,116
Sales allowance and other costs	27,027	22,257
Sales rebates and royalties	26,818	11,657
Accounts payable	6,538	15,282
Other	12,750	2,286
	$ 102,788	$ 76,446

7. Capitalization

In April 2018, the Company closed an underwritten public offering of its common stock pursuant to a registration statement on Form S-3. The Company issued and sold an aggregate of 4,600,000 shares of common stock under the registration statement at a public offering price of $27.04 per share, including 600,000 shares issued upon exercise by the underwriters of their option to purchase additional shares. The Company received net proceeds of approximately $117.9 million after deducting underwriting discounts and commissions and other offering expenses payable by the Company.

Warrants

All of the Company's outstanding warrants were classified as liabilities as of September 30, 2018 and December 31, 2017 because they contained non-standard antidilution provisions.

The following is a summary of the Company's outstanding warrants as of September 30, 2018 and December 31, 2017:

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

8. Net loss per share

Basic earnings per share is computed by dividing net loss by the weighted-average number of common shares outstanding. Diluted earnings per share is computed by dividing net loss by the weighted-average number of common shares plus the effect of any 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,	
	2018	2017	2018	2017
Numerator				
Net loss	$ (50,969)	$ (33,738)	$ (79,751)	$ (80,270)
Denominator				
Denominator for basic and diluted net loss per share	48,096,521	41,296,740	45,310,690	38,433,749
Net loss per share:				
Basic and diluted	$ (1.06) *	$ (0.82) *	$ (1.76) *	$ (2.09) *

*In the three and nine months ended September 30, 2018 and 2017, 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,	
	2018	2017
Stock Options	9,545,522	6,612,765
Unvested restricted stock awards and units	580,347	402,853
Total	10,125,869	7,015,618

9. 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 2009, the Company's shareholders approved 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, subject to certain adjustments and annual increases. 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. There are no additional shares available for issuance under this plan.

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, 2018, awards for 665,194 shares of common stock are available for issuance.

From January 1, 2018 through September 30, 2018, the Company issued a total of 2,914,139 stock options to various employees. Of those, 1,115,650 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 the Company's 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, 2017	6,448,642	$ 29.00		
Granted	2,914,139	$ 25.84		
Exercised	512,145	$ 17.03		
Forfeited/Cancelled	(329,404)	$ 34.20		
Outstanding at September 30, 2018	9,545,522	$ 28.44	7.45 years	$ 172,859
Vested or Expected to vest at September 30, 2018	3,914,413	$ 24.38	8.93 years	$ 89,547
Exercisable at September 30, 2018	4,316,071	$ 32.33	5.99 years	$ 77,003

The fair value of grants made in the nine months ended September 30, 2018 was contemporaneously estimated on the date of grant using the following assumptions:

	Nine months ended September 30, 2018
Risk-free interest rate	2.25%—3.03%
Expected volatility	64%—90%
Expected term	5.04 – 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, 2018 was $17.04 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, 2018	393,011	$ 15.64
Granted	354,691	$ 19.09
Vested	(113,795)	$ 16.36
Forfeited	(53,560)	$ 17.24
Unvested at September 30, 2018	580,347	$ 17.60

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 ended September 30, 2018, a total of 177,329 SARs vested. For the period ended September 30, 2018, the Company recorded $3.7 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 ended September 30, 2018, the Company recorded $0.7 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,	
	2018	2017	2018	2017
Research and development	$ 4,431	$ 3,624	$ 12,109	$ 11,986
Selling, general and administrative	4,511	3,544	12,664	12,096
Total	$ 8,942	$ 7,168	$ 24,773	$ 24,082

As of September 30, 2018, there was approximately $67.5 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 3.00 years.

10. Debt

2017 Credit Facility

In May 2017, the Company entered into a credit and security agreement (the "Credit Facility") with MidCap Financial Trust, a Delaware statutory trust (“MidCap”), as administrative agent and MidCap and certain other financial institutions as lenders thereunder (the “Credit Agreement”) that provides for a senior secured term loan facility of $60.0 million, of which $40.0 million was drawn by the Company on May 5, 2017. The remaining $20.0 million under the senior secured term loan facility will become available to the Company upon its demonstration (on or prior to December 31, 2018) of net product revenue equaling or exceeding $120.0 million for the trailing 12 month period. The Company capitalized approximately $0.4 million of debt issuance costs, which were netted against the carrying value of the Credit Facility and will be amortized over the term of the Credit Facility.

Borrowings under the Credit Agreement bear interest at a rate per annum equal to LIBOR (with a LIBOR floor rate of 1.00%) plus 6.15%. The Company is obligated to make interest only payments (payable monthly in arrears) through April 30, 2019. Commencing on May 1, 2019 and continuing for the remaining twenty-four months of the facility, the Company will be required to make monthly interest payments and monthly principal payments. The principal payments are to be made based on straight-line amortization of the principal over the twenty-four month period. The maturity date of the Credit Agreement is May 1, 2021, unless terminated earlier.

The Credit Facility is subject to certain financial covenants. As of September 30, 2018, the Company was in compliance with all required covenants.

Convertible 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 was not permitted to redeem the Convertible Notes prior to August 20, 2018. As of August 20, 2018, the Company may redeem for cash all or any portion of the Convertible Notes, at its option, 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. The equity component recorded at issuance related to the Convertible Notes is $57.5 million and was recorded in additional paid-in capital.

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, 2018**	**December 31, 2017**
Principal	$ 150,000	$ 150,000
Less: Debt issuance costs	(1,844)	(2,121)
Less: Debt discount, net(1)	(37,009)	(42,572)
Net carrying amount	$ 111,147	$ 105,307

(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 $172.9 million as of September 30, 2018. 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, 2018, the remaining contractual life of the Convertible Notes is approximately 3.9 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,	
	2018	2017	2018	2017
Contractual interest expense	$ 1,134	$ 1,134	$ 3,375	$ 3,375
Amortization of debt issuance costs	95	86	277	249
Amortization of debt discount	1,919	1,725	5,563	4,999
Total	$ 3,148	$ 2,945	$ 9,215	$ 8,623
Effective interest rate of the liability component	11%	11%	11%	11%

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 in connection with the Company's oncology and antibacterial programs. As the Company has discontinued development under its antibacterial program, it no longer expects that milestone and royalty payments from the Company to Wellcome Trust will apply under that agreement, resulting in a change to the total amount of development and regulatory milestone payments the Company may become obligated to pay for this program. Under the oncology program funding agreement, to the extent that the Company develops and commercializes program intellectual property on a for-profit basis itself or in collaboration with a partner (provided the Company retains overall control of worldwide commercialization), the Company may become obligated to pay to Wellcome Trust development and regulatory milestone payments 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. Additional milestone payments of up to an aggregate of $22.4 million may become payable by the Company to Wellcome Trust under this agreement.

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 is successfully developed and subsequently commercialized or, if the Company outlicenses rights to a collaboration product, a specified percentage of certain payments the Company receives from its 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 the Company's payment to the SMA Foundation of a specified amount.

Pursuant to the Merger Agreement with Agilis, the Company is required to pay $40.0 million of development milestone payments no later than the second anniversary of the closing of the Merger, regardless of whether the applicable milestones have been achieved. The Company may also be obligated to pay additional development, regulatory approval, and net sales milestones and net sales royalties. Refer to Note 3 for further details.

The Company also has a Collaboration and License Agreement with Akcea for the commercialization of Tegsedi and Waylivra, and products containing those compounds in countries in Latin America and the Caribbean. Pursuant to the agreement, the Company paid Akcea an upfront licensing fee, which included an initial payment of $12.0 million. An additional $6.0 million is payable within 30 days after receipt of regulatory approval of Waylivra from the FDA or the EMA, whichever occurs earlier. In addition, Akcea is eligible to receive milestone payments, on a Product-by-Product basis, of $4.0 million upon receipt of regulatory approval for a product from ANVISA, the Brazilian Health Regulatory Authority, subject to a maximum aggregate amount of $8.0 million for all such products. Akcea is also entitled to receive royalty payments subject to certain terms set forth in the Akcea Collaboration and License Agreement.

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. Additionally, the Company has royalty payments associated with Translarna and Emflaza product net sales, payable quarterly or annually in accordance with the terms of the related agreements.

In the period ended September 30, 2018, two lawsuits the Company was involved in were settled and dismissed (refer to Part II, Item 1. Legal Proceedings for further details on the dismissed lawsuits).

12. Revenue recognition

Net product sales

The Company views its operations and manages its business in one operating segment. During the three and nine months ended September 30, 2018, net product sales in the United States were $22.6 million and $62.2 million, respectively, consisting solely of Emflaza, and net product sales not in the United States were $30.4 million and $115.0 million, respectively, consisting solely of Translarna.

The following table presents changes in the Company's contract liabilities from December 31, 2017 to September 30, 2018:

	Balance as of December 31, 2017	Additions	Deductions	ASC 606 Adjustment	Balance as of September 30, 2018
Deferred Revenue	$ 11,891	$ 4,706	$ —	$ (3,937)	$ 12,660

The Company did not have any contract assets for the three and nine months ended September 30, 2018.

During the three and nine months ended September 30, 2018, the Company recognized revenue in the period from:

	Three Months Ended September 30, 2018	Nine Months Ended September 30, 2018
Amounts included in contract liabilities at the beginning of the period	$ —	$ —
Performance obligations satisfied in previous period	—	—
Performance obligations satisfied in current period	53,021	177,172
Total product revenue	$ 53,021	$ 177,172

The Company has not made significant changes to the judgments made in applying ASC Topic 606 for the three and nine months ended September 30, 2018.

Remaining performance obligations

Remaining performance obligations represent the transaction price for goods the Company has yet to provide. As of September 30, 2018, the aggregate amount of transaction price allocated to remaining performance obligations relating to Translarna net product revenue was $12.7 million. The Company expects to recognize revenue over the next one to three years as the specific timing for satisfying the performance obligations is contingent upon a number of factors, including customers' needs and schedules.

The impact of adoption using the modified retrospective method on the Company's consolidated financial statements is as follows:

i.Consolidated balance sheets

	Impact of changes in accounting policies		
	As reported September 30, 2018	Adjustments	As reported Balances without adoption of Topic 606
Assets			
Current assets:			
Cash and cash equivalents	$ 206,913	$ —	$ 206,913
Marketable securities	42,491	—	42,491
Trade receivables, net	42,197	—	42,197
Inventory	13,660	(84)	13,576
Prepaid expenses and other current assets	8,020	—	8,020
Total current assets	313,281	(84)	313,197
Fixed assets, net	8,805	—	8,805
Intangible assets, net	604,612	—	604,612
Goodwill	100,309	—	100,309
Deposits and other assets	1,620	—	1,620
Total assets	$ 1,028,627	$ (84)	$ 1,028,543
Liabilities and stockholders' equity			
Current liabilities:			
Accounts payable and accrued expenses	$ 102,788	$ (794)	$ 101,994
Current portion of long-term debt	6,667	—	6,667
Deferred revenue	2,004	5,120	7,124
Other current liabilities	3,463	—	3,463
Total current liabilities	114,922	4,326	119,248
Deferred revenue - long-term	11,156	—	11,156
Long-term debt	144,258	—	144,258
Contingent consideration payable	218,700	—	218,700
Deferred consideration payable	38,200	—	38,200
Deferred tax liability	115,200	—	115,200
Other long-term liabilities	101	—	101
Total liabilities	642,537	4,326	646,863
Stockholders' equity:			
Common stock	51	—	51
Additional paid-in capital	1,275,004	—	1,275,004
Accumulated other comprehensive income	1,628	—	1,628
Accumulated deficit	(890,593)	(4,410)	(895,003)
Total stockholders' equity	386,090	(4,410)	381,680
Total liabilities and stockholders' equity	$ 1,028,627	$ (84)	$ 1,028,543

ii.Consolidated statements of operations

	Impact of changes in accounting policies Three Months Ended		
	As reported for the period ended September 30, 2018	Adjustments	As reported Balances without adoption of Topic 606
Revenues:			
Net product revenue	$ 53,021	$ (834)	$ 52,187
Collaboration and grant revenue	570	—	570
Total revenues	53,591	(834)	52,757
Operating expenses:			
Cost of product sales, excluding amortization of acquired intangible asset	3,292	(17)	3,275
Amortization of acquired intangible asset	5,793	—	5,793
Research and development	54,368	—	54,368
Selling, general and administrative	38,368	—	38,368
Total operating expenses	101,821	(17)	101,804
Loss from operations	(48,230)	(817)	(49,047)
Interest expense, net	(3,118)	—	(3,118)
Other expense, net	734	—	734
Loss before income tax expense	(50,614)	(817)	(51,431)
Income tax expense	(355)	—	(355)
Net loss attributable to common stockholders	$ (50,969)	$ (817)	$ (51,786)

	Impact of changes in accounting policies Year to Date		
	As reported for the period ended September 30, 2018	Adjustments	As reported Balances without adoption of Topic 606
Revenues:			
Net product revenue	$ 177,172	$ (1,059)	$ 176,113
Collaboration and grant revenue	1,224	—	1,224
Total revenues	178,396	(1,059)	177,337
Operating expenses:			
Cost of product sales, excluding amortization of acquired intangible asset	8,909	(84)	8,825
Amortization of acquired intangible asset	16,815	—	16,815
Research and development	118,337	—	118,337
Selling, general and administrative	104,882	—	104,882
Total operating expenses	248,943	(84)	248,859
Loss from operations	(70,547)	(975)	(71,522)
Interest expense, net	(9,306)	—	(9,306)
Other income, net	1,066	—	1,066
Loss before income tax expense	(78,787)	(975)	(79,762)
Income tax expense	(964)	—	(964)
Net loss attributable to common stockholders	$ (79,751)	$ (975)	$ (80,726)

iii.Consolidated statements of comprehensive loss

	Impact of changes in accounting policies Three Months Ended		
	As reported for the period ended September 30, 2018	Adjustments	As reported Balances without adoption of Topic 606
Net loss	$ (50,969)	$ (817)	$ (51,786)
Other comprehensive loss:			
Unrealized gain on marketable securities, net of tax	33	—	33
Foreign currency translation loss	(260)	—	(260)
Comprehensive loss	$ (51,196)	$ (817)	$ (52,013)

	Impact of changes in accounting policies Year to Date		
	As reported for the period ended September 30, 2018	Adjustments	As reported Balances without adoption of Topic 606
Net loss	$ (79,751)	$ (975)	$ (80,726)
Other comprehensive loss:			
Unrealized loss on marketable securities, net of tax	(50)	—	(50)
Foreign currency translation loss	(2,291)	—	(2,291)
Comprehensive loss	$ (82,092)	$ (975)	$ (83,067)

iv.Consolidated statements of cash flows

	Impact of changes in accounting policies		
	As reported for the period ended September 30, 2018	Adjustments	Balances without adoption of Topic 606
Cash flows from operating activities			
Net loss	$ (79,751)	$ (975)	$ (80,726)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	19,316	—	19,316
Change in valuation of warrant liability	3	—	3
Non-cash interest expense	5,563	—	5,563
Loss on disposal of asset	2	—	2
Amortization of premiums and accretion of discounts on investments, net	(354)	—	(354)
Amortization of debt issuance costs	390	—	390
Share-based compensation expense	24,773	—	24,773
Unrealized foreign currency transaction gain	(977)	—	(977)
Changes in operating assets and liabilities:			
Inventory, net	(3,252)	(84)	(3,336)
Prepaid expenses and other current assets	(1,301)	—	(1,301)
Trade receivables, net	(2,681)	—	(2,681)
Deposits and other assets	(385)	—	(385)
Accounts payable and accrued expenses	18,606	(794)	17,812
Other liabilities	1,617	—	1,617
Deferred revenue	5,933	1,853	7,786
Net cash used in operating activities	(12,498)	—	(12,498)
Cash flows from investing activities			
Purchases of fixed assets	(2,489)	—	(2,489)
Purchases of marketable securities	(28,656)	—	(28,656)
Sale and redemption of marketable securities	65,923	—	65,923
Acquisition of product rights	(3,903)	—	(3,903)
Business acquisition, net of cash acquired	(48,892)	—	(48,892)
Net cash (used in) / provided by investing activities	(18,017)	—	(18,017)
Cash flows from financing activities			
Proceeds from exercise of options	8,631	—	8,631
Net proceeds from public offerings	117,915	—	117,915
Proceeds from shares issued under employee stock purchase plan	1,299	—	1,299
Net cash provided by financing activities	127,845	—	127,845
Effect of exchange rate changes on cash	(2,209)	—	(2,209)
Net increase in cash and cash equivalents	95,121	—	95,121
Cash and cash equivalents, beginning of period	111,792	—	111,792
Cash and cash equivalents, end of period	$ 206,913	$ —	$ 206,913

Collaboration revenue

The Company has ongoing collaborations with the Spinal Muscular Atrophy Foundation (SMA Foundation) and F. Hoffman-La Roche Ltd and Hoffman- La Roche Inc. (collectively, Roche) and early stage discovery arrangements with other institutions. The following are the key terms to the Company's (i) ongoing collaborations and (ii) early stage discovery and development arrangements.

Roche and SMA Foundation

In November 2011, the Company and the SMA Foundation entered into a licensing and collaboration agreement with Roche for a spinal muscular atrophy program. Under the terms of the agreement, Roche acquired an exclusive worldwide license to the Company's spinal muscular atrophy program, which includes three compounds currently in preclinical development, as well as potential back-up compounds. The Company received a nonrefundable upfront cash payment of $30.0 million during the research term, which was terminated effective December 31, 2014, after which Roche provided the Company with funding, based on an agreed- upon full-time equivalent rate, for an agreed-upon number of full- time equivalent employees that the Company contributed to the research program.

The Company identified two material promises in the collaboration agreement, the license and the research activities. The Company evaluated whether these material promises are distinct and determined that the license does not have standalone functionality and there is a significant integration of the license and research activities. As such, both promises were bundled into one distinct performance obligation. As a result, the Company deferred the $30.0 million upfront payment which was recognized over the estimated performance period of two years, which was the contracted research period. As of adoption of ASC Topic 606 on January 1, 2018, all performance obligations had been satisfied and the balance of the remaining deferred upfront payment was fully recognized.

Under the agreement, the Company is eligible to receive additional payments from Roche if specified events are achieved with respect to each licensed product, including up to $135.0 million in research and development event milestones, up to $325.0 million in sales milestones upon achievement of sales events, and up to double digit royalties on worldwide annual net sales of a commercial product.

In August 2013, a lead development compound, RG7800, was selected to move into IND-enabling studies, which triggered a milestone payment to the Company from Roche of $10 million. Under ASC Topic 605, the Company considered this milestone event substantive because the applicable criteria of its revenue recognition policy would be satisfied and recorded it as collaboration revenue for the year ended December 31, 2013.

In January 2014, the Company announced the initiation of a Phase 1 clinical program in its spinal muscular atrophy collaboration with Roche and the SMA Foundation which triggered a $7.5 million milestone payment from Roche. Under ASC Topic 605, the Company considered this milestone event substantive because the applicable criteria of its revenue recognition policy would be satisfied and recorded it as collaboration revenue for the year ended December 31, 2014.

In November 2014, the Company announced the initiation of a Phase 2 study in adult and pediatric patients in its spinal muscular atrophy collaboration with Roche and the SMA Foundation which triggered a $10 million payment from Roche. Under ASC Topic 605, the Company considered this milestone event substantive because the applicable criteria of its revenue recognition policy would be satisfied and recorded it as collaboration revenue for the year ended December 31, 2014.

In October 2017, the Company announced that the Sunfish, a two-part clinical trial in pediatric and adult type 2 and type 3 spinal muscular atrophy initiated in the fourth quarter of 2016 with Roche and SMA Foundation, had transitioned into the pivotal second part of its study. The achievement of this milestone triggered a $20.0 million payment to the Company from Roche. Under ASC Topic 605, the Company considered this milestone event substantive because the applicable criteria of its revenue recognition policy would be satisfied and recorded it as collaboration revenue for the year ended December 31, 2017.

The remaining potential research and development event milestones that can be received as of September 30, 2018 is $87.5 million.

For the nine months ended September 30, 2018 and 2017, the Company recognized revenue related to the licensing and collaboration agreement with Roche of $0.2 million and $0.2 million, respectively.

Early stage collaboration and discovery agreements

From time to time, the Company has arrangements with several organizations pursuant to which the Company uses its discovery technologies to help identify potential drug candidates. The Company does not take ownership of the potential compounds, but rather provides research services to the collaborator using its specialized technology platform.

Generally, these arrangements are structured such that the collaborator and the Company work together to jointly select targets from which to apply its discovery technologies. The research period for the Company to apply its technology is generally three to four years. The Company will typically receive a nonrefundable, upfront cash payment and the collaborator agrees to provide funding for research activities performed on its behalf.

Generally, the two material promises in these arrangements are the license and the research activities. The Company evaluated whether these material promises are distinct and determined that the license does not have standalone functionality and there is a significant integration of the license and research activities. As such, both promises are bundled into one distinct performance obligation. As of adoption of ASC Topic 606 on January 1, 2018, all deferred revenue related to these arrangements had been

recognized. For the nine months ended September 30, 2018 and 2017, the Company did not recognize any revenue related to discovery agreements.

The Company is eligible to receive additional payments from its early stage discovery research arrangements if the discovery compounds are ultimately developed and commercialized. The aggregate potential payments the Company is eligible for if all products are developed is $143.0 million and up to $252.0 million in sales milestones upon achievement of specified sales events and up to double digit royalties on worldwide annual net sales of the licensed product. The Company will recognize revenue when it is probable the milestones will be achieved (see Note 2). For the nine months ended September 30, 2018 and 2017, the Company did not recognize any revenue related to early stage collaborations.

13. Intangible assets and goodwill

Definite-lived intangibles

On April 20, 2017, the Company completed its previously announced acquisition of all rights to Emflaza pursuant to the Asset Purchase Agreement, dated March 15, 2017, and amended on April 20, 2017, by and between the Company and Marathon. The assets acquired by the Company in the Transaction include intellectual property rights related to Emflaza, inventories of Emflaza, and certain contractual rights related to Emflaza. In accordance with ASU No. 2017-01, the Company determined that substantially all of the fair value is concentrated in the Emflaza rights intangible asset and as such accounted for the transaction as an asset acquisition under ASC 805-50 and recorded an intangible asset of $148.4 million.

The Emflaza rights intangible asset is being amortized to cost of product sales over its expected useful life of approximately seven years on a straight line basis.

Marathon is entitled to receive contingent payments from the Company based on annual net sales of Emflaza beginning in 2018, up to a specified aggregate maximum amount over the expected commercial life of the asset. In accordance with the guidance for an asset acquisition, the Company will record the milestone payment when it becomes payable to Marathon and increase the cost basis for the Emflaza rights intangible asset.

For the three and nine month periods ended September 30, 2018, the Company recorded $4.5 million and $8.4 million of milestone payments, respectively, which were added to the cost basis for the Emflaza rights intangible asset and will be amortized prospectively on a straight-line basis over the remaining life of the asset. As of September 30, 2018, the $4.5 million milestone payment was recorded on the balance sheet within accrued expenses as a contingent payment payable to Marathon.

For the three and nine months ended September 30, 2018, the Company recognized amortization expense of $5.8 million and $16.8 million, respectively, related to the Emflaza rights intangible asset. The estimated future amortization of the Emflaza rights intangible asset is expected to be as follows:

	As of September 30, 2018
2018(1)	$ 5,794
2019	23,172
2020	23,172
2021	23,172
2022 and thereafter	49,302
Total	$ 124,612

(1) For the three months ended December 31, 2018.

Indefinite-lived intangibles

In connection with the acquisition of Agilis (Note 3), the Company acquired rights to PTC-AADC, for the treatment of AADC deficiency. AADC deficiency is a rare CNS disorder arising from reductions in the enzyme AADC that result from mutations in the dopa decarboxylase gene. The Agilis platform also includes a gene therapy asset targeting Friedreich ataxia, a rare and life-shortening neurodegenerative disease caused by a single defect in the FXN gene which causes reduced production of the frataxin protein. An investigational new drug ("IND") submission with the FDA for this program is expected in 2019. Additionally, the Agilis platform includes two other gene therapy programs targeting CNS disorders, including Angelman syndrome, a rare, genetic, neurological disorder characterized by severe developmental delays.

In accordance with the acquisition method of accounting, the Company allocated the acquisition cost for the Merger to the underlying assets acquired and liabilities assumed, based upon the estimated fair values of those assets and liabilities at the date of acquisition. The Company classified the fair value of the acquired IPR&D as indefinite lived intangible assets until the successful completion or abandonment of the associated research and development efforts. The preliminary value allocated to the indefinite lived intangible assets was $480 million.

Goodwill

As a result of the Merger on August 23, 2018, the Company recorded $100.3 million of goodwill. There were no changes to the recorded value of goodwill for the three and nine month periods ended September 30, 2018.

Collaboration and Licensing Agreement

On August 1, 2018, the Company entered into a Collaboration and License Agreement with Akcea for the commercialization of Tegsedi and Waylivra, and products containing those compounds in countries in Latin America and the Caribbean. Pursuant to the agreement, the Company paid Akcea an upfront licensing fee, which included an initial payment of $12.0 million. An additional $6.0 million is payable within 30 days after receipt of regulatory approval of Waylivra from the United States Food and Drug Administration or the European Medicines Agency, whichever occurs earlier. The Company evaluated the agreement under the guidance in ASC 730 and concluded that the acquired rights to commercialize the products had no alternative future use as of the date of the Merger. Accordingly, the $12.0 million was charged to research and development expense in the consolidated statements of operations for the three and nine month periods ended September 30, 2018. The Company plans to a file a request for marketing authorizations for Tegsedi with ANVISA in the first half of 2019. Waylivra is currently under regulatory review in the EU.

14. 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, 2017 included in our Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 6, 2018. 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, Part I, Item 1A. (Risk Factors) of our Annual Report on Form 10-K for the year ended December 31, 2017, Part II, Item 1A. (Risk Factors) of our Quarterly Reports on Form 10-Q for the periods ended March 31, 2018 and June 30, 2018, and Exhibit 99.2 to our Current Report on Form 8-K filed on August 24, 2018 and our actual results may differ materially from those anticipated in these forward-looking statements.

Our Company

We are a science-led global biopharmaceutical company focused on the discovery, development and commercialization of clinically-differentiated medicines that provide benefits to patients with rare disorders. Our ability to globally commercialize products is the foundation that drives our continued investment in a robust pipeline of transformative medicines and our mission to provide access to best-in-class treatments for patients who have an unmet medical need. Our strategy is to bring best-in-class therapies with differentiated clinical benefit to patients affected by rare disorders and to leverage our global commercial infrastructure to maximize value for our patients and other stakeholders.

We have two products, Translarna™ (ataluren) and Emflaza™ (deflazacort), for the treatment of Duchenne muscular dystrophy, or DMD, a rare, life threatening disorder. During the quarter ended September 30, 2018, we recognized $30.4 million in sales of Translarna. Translarna is currently available for the treatment of nmDMD in over 25 countries on a commercial basis or through a reimbursed early access program, or EAP program. We hold worldwide commercialization rights to Translarna for all indications in all territories. Emflaza is approved in the United States for the treatment of DMD in patients five years and older. During the quarter ended September 30, 2018, Emflaza achieved sales of $22.6 million.

We have a pipeline of gene therapy product candidates, including PTC-AADC for the treatment of Aromatic L-Amino Acid Decarboxylase, or AADC, deficiency, or AADC deficiency. We are preparing a biologics license application, or BLA, for PTC-AADC for the treatment of AADC deficiency in the United States, which we anticipate submitting to the U.S. Food and Drug

Administration, or FDA, in 2019. We are also preparing a marketing authorisation application, or MAA, for PTC-AADC for the treatment of AADC deficiency in the European Union, or EU, which we anticipate submitting to the European Medicines Agency, or EMA, in 2019, as well. We hold the rights for the commercialization of Tegsedi™ (inotersen) and Waylivra™ (volanesorsen) for the treatment of rare diseases in countries in Latin America and the Caribbean. Tegsedi has received marketing authorization in the U.S., EU and Canada for the treatment of stage 1 or stage 2 polyneuropathy in adult patients with hereditary transthyretin amyloidosis, or hATTR amyloidosis. We plan to file a request for marketing authorization for Tegsedi with ANVISA, the Brazilian Health Regulatory Authority, in the first half of 2019. Waylivra is currently under regulatory review in the EU for the treatment of familial chylomicronemia syndrome, or FCS.

We also have a spinal muscular atrophy (SMA) collaboration 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. Currently, our collaboration has three clinical trials ongoing to evaluate the safety and effectiveness of risdiplam (RG7916, RO7034067), the lead compound in the SMA program. In addition, we have a pipeline of product candidates that are in early clinical and pre-clinical development. Our pre-clinical and discovery programs are focused on the development of new treatments for multiple therapeutic areas, including rare diseases and oncology.

Corporate Updates

Acquisition of Agilis Biotherapeutics, Inc.

On August 23, 2018, we completed our acquisition of Agilis Biotherapeutics, Inc., or Agilis, pursuant to an Agreement and Plan of Merger, dated as of July 19, 2018, or the Merger Agreement, by and among us, Agility Merger Sub, Inc., a Delaware corporation and our wholly owned, indirect subsidiary, Agilis and, solely in its capacity as the representative, agent and attorney-in-fact of the equityholders of Agilis, Shareholder Representative Services LLC, or the Merger.

Upon the closing of the Merger, we paid to Agilis equityholders total upfront consideration comprised of $49.2 million in cash and 3,500,907 shares of our common stock, or the Closing Stock Consideration. The Closing Stock Consideration was determined by dividing $150.0 million by the volume-weighted average price per share of our common stock on the Nasdaq Global Select Market for the 10 consecutive trading-day period ending on the second trading-day immediately preceding the closing of the Merger. Agilis equityholders may become entitled to receive contingent payments from us based on the achievement of certain development, regulatory and net sales milestones as well as based upon a percentage of net sales of certain products. Under the Merger Agreement, we are required to pay $40.0 million of the development milestone payments no later than the second anniversary of the closing of the Merger, regardless of whether the applicable milestones have been achieved.

The completion of the Merger gives us a gene therapy platform focused on the development of innovative therapies for rare, debilitating diseases of the central nervous system, or CNS. Our lead gene therapy product candidate is PTC-AADC for the treatment of AADC deficiency. AADC deficiency is a rare CNS disorder arising from reductions in the enzyme AADC that result from mutations in the dopa decarboxylase gene. AADC is the enzyme responsible for the conversion of L-dopa to dopamine. Dopamine is a key neurotransmitter that acts within the striatum (caudate and putamen), a component of the brain's deep grey matter, to modulate output of neurons that project to the motor and premotor cortices of the brain that plan and execute normal motor function and is required to be present in the brain for humans to develop and maintain proper motor function.

AADC deficiency is a monogenic disorder of neurotransmitter synthesis that manifests in young children and most commonly results in profound developmental delay, often seen as complete arrest of motor development. AADC deficiency generally causes the inability to develop motor control (global muscular hypotonia/dystonia), resulting in breathing, feeding, and swallowing problems, frequent hospitalizations, and the need for life-long care. On average, patients with AADC deficiency die in the first decade of life due to profound motor dysfunction and secondary complications such as choking, hypoxia, and pneumonia. Currently, no treatment options are available for the underlying cause of the disorder, and care is limited to palliative options with significant burden on caregivers.

The prevalence of AADC deficiency has been estimated to be approximately 5,000 patients worldwide, with a live-birth incidence of approximately 1 in 40,000 worldwide. While several diagnostic tests for AADC deficiency are available, the condition remains largely misdiagnosed or undiagnosed.

PTC-AADC is a large molecule, adeno-associated virus (AAV) gene therapy, which has been assessed in two completed clinical trials, and one trial in which enrollment and dosing is ongoing. The two completed trials include a total of 18 children with severe AADC deficiency who were treated with a one-time total dose of 1.8×10^{11} vg of PTC-AADC during a single procedure in which the gene therapy was administered directly to the region of the brain where dopamine is made, called the putamen. The targeted micro-dosing approach administering small amounts of gene therapy directly to focal regions of affected cells in the putamen has the benefit of keeping the supply requirements for materials low, improving access of the therapeutic gene to key cells, potentially limiting immune and complement-mediated responses and reducing the risk of off-target uptake and secretion and excretion of

the gene therapy by the liver and kidneys. To date, results from these trials suggest that patients may have a gain of motor functions and improvement in cognitive scales following gene therapy administration and have shown significant increases in motor function, which contrasts with the published natural history.

The two completed trials, AADC-1601, a trial in which patients were enrolled under individual compassionate use consents, and AADC-010, were both single-arm, open-label, interventional trials that enrolled a total of 18 patients. The primary and secondary endpoints of these trials were to assess the safety and efficacy of PTC-AADC administered via bilateral putaminal- infusions in patients with severe AADC deficiency at a total one-time dose of 1.8×10^{11} vg. Study enrollment required a diagnosis of AADC deficiency, defined as decreased homovanilic acid, or HVA, and 5-hydroxyindoleacetic acid, or 5-HIAA, and elevated L-Dopa cerebrospinal fluid, or CSF, levels, presence of more than one DDC gene mutation, and presence of clinical symptoms of AADC deficiency (including developmental delay, hypotonia, dystonia, and oculogyric crisis), and patient age of older than 2 years.

Patients were evaluated monthly for safety assessments and every three months for efficacy assessments that included tests of motor developmental testing (Peabody Developmental Motor Scale, Second Edition, or PDMS-2, and Alberta Infant Motor Scale, or AIMS) through the first year after treatment with PTC-AADC and at periodic intervals thereafter through five years following treatment. The PDMS-2 and AIMS are validated scales used to assess motor skills in young children. Pharmacodynamic testing of CNS AADC activity over time included analyses of CSF neurotransmitter metabolites and FDOPA PET imaging intervals, also through five years.

8 patients were enrolled in the AADC-1601 study. 10 patients were enrolled in the AADC-010 study. In both studies, the average age of patients was less than 5 years of age.

At baseline, patients had no functional movement and failed to achieve any motor milestones, including head control, sitting or standing capabilities, consistent with the published natural history of severe AADC deficiency. Compared to baseline, at one-year and at five-years after PTC-AADC administration, patients had objective evidence of de novo dopamine production as visualized by F-DOPA PET imaging of the brain, consistent with successful and stable gene expression and enzyme activity over time.

Based on preliminary analysis, following administration of PTC-AADC, the combined group of patients showed significant changes from baseline capabilities at one-year post-treatment in functional motor skills assessed with the PDMS-2 total score, as well as locomotion, grasping, visual-motor integration and stationary subscales. Significant changes from baseline at one-year post-treatment were also observed for the combined group of patients on the AIMS total score and prone, supine, sit and stand subscales.

Compared to published natural history data, patients in these trials showed statistically significant improvements at both two- and five-years post-treatment in achievement of motor milestones of full head control (at 2 and 5 years), sitting unassisted (at 2 and 5 years) and standing with support (at 5 years), reinforcing the clinical benefit and sustainability of functional motor improvements.

Surgical injection of PTC-AADC in both completed trials was well tolerated, with no adverse events occurring during the surgical procedure. Adverse events were generally associated with the disease state. The most frequent adverse event associated with PTC-AADC was dyskinesia and these events completely resolved over time. No serious adverse events have been attributed to PTC-AADC.

The ongoing clinical trial, AADC-011, is a single-center, open-label trial to assess the efficacy and safety of PTC-AADC in patients with AADC deficiency. The primary outcomes for this trial include assessing a change in the PDMS-2 score and measuring the change in the neurotransmitter metabolite homovanillic acid (HVA) or 5-hydroxyindoleacetic acid (HIAA) in the cerebrospinal fluid.

An end-of-phase 2 meeting was held with the FDA in July 2017, and the clinical, non-clinical and manufacturing data available to date from the two completed clinical trials was reviewed. The FDA provided feedback indicating that the clinical and non-clinical data available to date was sufficient to support the submission of a BLA without undertaking additional trials or studies at this time. Based on the FDA input, including with respect to manufacturing, we are preparing a BLA for PTC-AADC for the treatment of AADC deficiency in the United States, which we anticipate submitting to the FDA in 2019. PTC-AADC for the treatment of AADC deficiency has orphan drug designation in the United States and European Union, and rare pediatric disease designation in the United States, and upon BLA approval the FDA may grant us a priority review voucher.

In April 2018, a protocol assistance meeting was held with the Scientific Advice Working Party of the European Medicines Agency, or EMA, in anticipation of the expected submission of a marketing authorisation application, or MAA, in the European Union and feedback was received indicating that the clinical and non-clinical data available to date was sufficient to support the submission of an MAA without undertaking additional trials or studies at this time. We expect to prepare and submit to the EMA an MAA for the treatment of AADC deficiency with PTC-AADC in the European Union during 2019. Based on the FDA input and feedback from the EMA, we do not deem necessary and do not plan to conduct a Phase 3 trial for PTC-AADC for the treatment of AADC deficiency.

There is no guarantee that we will be able to make the BLA or MAA submissions within our expected timelines or that following such submissions, the FDA or EMA would not have additional comments or requirements with respect to the respective submissions that we would be required to address before obtaining regulatory approval, or that the FDA, the EMA or any other regulatory authority will approve PTC-AADC for treatment of AADC deficiency at all.

If PTC-AADC for the treatment of AADC deficiency receives FDA approval, we expect that PTC-AADC would have a twelve-year exclusive marketing period in the United States for the approved indication, commencing on the date of FDA approval, under the provisions of the Biologics Price Competition and Innovation Act of 2009, or BPCIA, as well as a concurrent seven-year exclusive marketing period, which would commence on the date of FDA approval, under the provisions of the Orphan Drug Act of 1983, or the Orphan Drug Act. We are pursuing patent protection for PTC-AADC, and, in the meantime, we expect to rely on the twelve-year BPCIA regulatory exclusivity and concurrent seven-year Orphan Drug Act exclusivity to commercialize PTC-AADC in the United States, if it is approved.

Our gene therapy platform also includes a gene therapy asset targeting Friedreich ataxia, a rare and life-shortening neurodegenerative disease caused by a single defect in the FXN gene which causes reduced production of the frataxin protein. An investigational new drug, or IND, submission with the FDA for this program is expected in 2019. Additionally, the gene therapy platform includes two other gene therapy programs targeting CNS disorders, including Angelman syndrome, a rare, genetic, neurological disorder characterized by severe developmental delays.

Bridge Loan and Security Agreement

In connection with the Merger Agreement, on July 19, 2018, we entered into a Bridge Loan and Security Agreement, or the Bridge Loan Agreement, by and among us, Agilis and certain of Agilis's domestic subsidiaries, as guarantors. Under the Bridge Loan Agreement, we made a term loan advance to Agilis on July 23, 2018 in an original principal amount of $10.0 million. In connection with the closing of the Merger, the original principal amount of $10.0 million plus all accrued and unpaid interest thereon was credited against the cash portion of the upfront consideration paid by us pursuant to the terms of the Merger Agreement in satisfaction of Agilis's outstanding payment obligations under the Bridge Loan Agreement, and we will have no further obligation to extend any further loan amounts under the Bridge Loan Agreement.

Akcea Collaboration and Licensing Agreement

On August 1, 2018, or the Effective Date, PTC Therapeutics International Limited, or PTC International, our subsidiary, entered into a Collaboration and License Agreement, or the Akcea Agreement, with Akcea Therapeutics, Inc., or Akcea, for the commercialization by PTC International of Tegsedi™ (inotersen), WAYLIVR™ (volanesorsen) and products containing those compounds, which we refer to collectively as the Products, in countries in Latin America and the Caribbean, or the PTC Territory.

Under the terms of the Akcea Agreement, Akcea has granted to PTC International an exclusive right and license, with the right to grant certain sublicenses, under Akcea's product-specific intellectual property to develop, manufacture and commercialize the Products in the PTC Territory. In addition, Akcea has granted to PTC International a non-exclusive right and license, with the right to grant certain sublicenses, under Akcea's core intellectual property and manufacturing intellectual property to develop, manufacture and commercialize the Products in the PTC Territory and to manufacture the Products worldwide in accordance with a supply agreement with Akcea. Akcea has in-licensed certain of the Akcea intellectual property from its affiliate, Ionis Pharmaceuticals, Inc., or Ionis. Each party has agreed not to, independently or with any third party, commercialize any competing oligonucleotide product in the PTC Territory for the same gene target as inotersen.

PTC International agreed to pay to Akcea an upfront licensing fee of $18.0 million, consisting of an initial payment of $12.0 million paid in connection with entering into the Akcea Agreement, and $6.0 million to be paid within 30 days after receipt of regulatory approval of Waylivra from the FDA or the EMA, whichever occurs earlier. In addition, Akcea is eligible to receive milestone payments, on a Product-by-Product basis, of $4.0 million upon receipt of regulatory approval for a Product from ANVISA, the Brazilian Health Regulatory Authority, subject to a maximum aggregate amount of $8.0 million for all such Products. Akcea is also entitled to receive royalty payments in the mid-twenty percent range of net sales on a country-by-country and Product-by-Product basis, commencing on the earlier to occur of (1) 12 months after the first commercial sale of such Product in Brazil or (2) the date when PTC International, its affiliates or sublicensees have recognized revenue of $10.0 million or more in cumulative net sales for such Product in the PTC Territory. The royalty payments are subject to reduction in certain circumstances as set forth in the Akcea Agreement.

Tegsedi, a product of Ionis' proprietary antisense technology, is an antisense oligonucleotide, or ASO, inhibitor of human transthyretin, or TTR, production. Tegsedi is the world's first RNA-targeted therapeutic to treat patients with hereditary transthyretin amyloidosis (hATTR amyloidosis). It has received marketing authorization in the U.S., EU and Canada for the treatment of stage 1 or stage 2 polyneuropathy in adult patients with hATTR amyloidosis. We plan to file a request for marketing authorization with ANVISA in the first half of 2019.

hATTR amyloidosis is a progressive, systemic and fatal inherited disease caused by the abnormal formation of the TTR protein and aggregation of TTR amyloid deposits in various tissues and organs throughout the body, including in peripheral nerves, heart, intestinal tract, eyes, kidneys, central nervous system, thyroid and bone marrow. The progressive accumulation of TTR amyloid deposits in these tissues and organs leads to sensory, motor and autonomic dysfunction often having debilitating effects on multiple aspects of a patient's life. Patients with hATTR amyloidosis often present with a mixed phenotype and experience overlapping symptoms of polyneuropathy and cardiomyopathy.

Ultimately, hATTR amyloidosis generally results in death within three to fifteen years of symptom onset. Therapeutic options for the treatment of patients with hATTR amyloidosis are limited and there are currently no disease-modifying drugs approved for the disease. There are an estimated 50,000 patients with hATTR amyloidosis worldwide, including approximately 6,000 patients with polyneuropathic hATTR amyloidosis in Latin America.

Waylivra, is under regulatory review in the EU for the treatment of familial chylomicronemia syndrome, or FCS. The U.S. and EU regulatory agencies have granted Orphan Drug Designation to Waylivra for the treatment of FCS. In August 2018, Waylivra received a Complete Response Letter from the FDA's Division of Metabolism and Endocrinology Products. In the coming weeks, Waylivra will be receiving a notice of noncompliance withdrawal letter from Health Canada. Additionally, Waylivra is currently in Phase 3 clinical development for the treatment of people with familial partial lipodystrophy, or FPL. The EMA has granted orphan drug designation to Waylivra for the treatment of patients with FPL.

FCS is an ultra-rare disease caused by impaired function of the enzyme lipoprotein lipase (LPL) and characterized by severe hypertriglyceridemia (>880mg/dL) and a risk of unpredictable and potentially fatal acute pancreatitis. Because of limited LPL function, people with FCS cannot break down chylomicrons, lipoprotein particles that are 90% triglycerides. In addition to pancreatitis, FCS patients are at risk of chronic complications due to permanent organ damage. They can experience daily symptoms including abdominal pain, generalized fatigue and impaired cognitions that affect their ability to work. People with FCS also report major emotional and psychosocial effects including anxiety, social withdrawal, depression and brain fog. There is no effective therapy for FCS currently available.

Neither Tegsedi nor Waylivra is currently approved for marketing in the PTC Territory.

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

United States. Translarna is an investigational new drug in the U.S. During the first quarter of 2017, we filed a New Drug Application, or NDA, for Translarna for the treatment of nmDMD over protest with the FDA. In October 2017, the Office of Drug Evaluation I of the FDA issued a Complete Response Letter for the NDA, stating that it was unable to approve the application in its current form. In response, we filed a formal dispute resolution request with the Office of New Drugs of the FDA. In February 2018, the Office of New Drugs of the FDA denied our appeal of the Complete Response Letter. In its response, the Office of New Drugs recommended a possible path forward for our ataluren NDA submission based on the accelerated approval pathway. This would involve a re-submission of an NDA containing the current data on effectiveness of ataluren with new data to be generated on dystrophin production in nmDMD patients' muscles. We intend to follow the FDA's recommendation and will collect such dystrophin data using newer technologies via procedures and methods that we are currently designing and expect to initiate such a study by the end of 2018. Additionally, should a re-submission of an NDA receive accelerated approval, the Office of New Drugs stated that Study 041, which is currently enrolling, could serve as the confirmatory post-approval trial required in connection with the accelerated approval pathway.

There is substantial risk that the studies we use to collect the dystrophin data will not provide the necessary data to support a marketing approval for Translarna for the treatment of nmDMD.

European Economic Area. In July 2018, the European Commission renewed our marketing authorization for Translarna for the treatment of nmDMD in ambulatory patients aged two years and older in the 31 member states of the European Economic Area, or EEA, and it is effective, unless extended, through August 5, 2019. We received initial marketing authorization from the European Commission in August 2014 for the treatment of nmDMD in ambulatory patients aged five years and older. In July 2018, the European Commission approved a label-extension request to our marketing authorization for Translarna in the EEA to include patients from two to up to five years of age. In September 2018, we submitted to the EMA a label-extension request to our marketing authorization in the EEA to include patients who are non-ambulatory. However, there can be no assurances that we will successfully obtain such label extension.

The marketing authorization is subject to annual review and renewal by the European Commission following reassessment by the EMA of the benefit-risk balance of continued authorization, which we refer to as the annual EMA reassessment, as well as our satisfaction of any specific obligation or other requirement placed upon the marketing authorization, including Study 041. Study 041 is a three-year clinical trial to confirm the efficacy and safety of Translarna in the approved patient population. The trial is comprised of two stages: an 18-month randomized, double-blind, placebo controlled clinical trial followed by an 18-month open label extension period. We expect to submit the results of Study 041 to the EMA by the end of the third quarter of 2021. We expect that as part of the annual EMA assessment, the EMA will consider the ongoing status of Study 041. There is substantial risk that

if we are unable to renew our EEA marketing authorization during any annual renewal cycle, if our product label is materially restricted, or if Study 041 does not provide the data necessary to maintain our marketing authorization, we would lose all, or a significant portion of, our ability to generate revenue from sales of Translarna in the EEA and other territories.

Each country, including each member state of the EEA, has its own pricing and reimbursement regulations and system. In order to commence commercial sale of product pursuant to our Translarna marketing authorization in any particular country in the EEA, we must finalize pricing and reimbursement negotiations with the applicable government body in such country. As a result, our commercial activities will continue to be on a country-by-country basis. We also have made, and expect to continue to make, product available under EAP programs, both in countries in the EEA and other territories. Our ability to negotiate, secure and maintain reimbursement for product under commercial and EAP programs can be subject to challenge in any particular country and can also be affected by political, economic and regulatory developments in such country.

Emflaza for the treatment of Duchenne muscular dystrophy in the United States

Emflaza, both in tablet and suspension form, received approval from the FDA in February 2017 as a treatment for DMD in patients five years of age and older in the United States. We estimate that there are approximately 10,000 DMD patients in the United States aged five years or older. We are obligated to complete certain post-marketing requirements in connection with the FDA's approval, including pre-clinical and clinical safety studies.

We expect that Emflaza will have a seven-year exclusive marketing period in the United States for the approved indication, commencing on the date of FDA approval, under the provisions of the Orphan Drug Act as well as a concurrent five-year exclusive marketing period in the United States for the active ingredient in Emflaza under the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act. Additionally, because the FDA has requested that we conduct a pediatric study of Emflaza, we expect to be granted a term of pediatric exclusivity upon completion of an agreed-upon study. This additional exclusivity would provide for an additional six months of marketing protection beginning as of the end of the term of any existing regulatory exclusivity, including the seven-year orphan exclusivity period. As we presently have no patent rights to protect the approved use of Emflaza, we expect to rely on both the five-year Hatch-Waxman Act and seven-year Orphan Drug Act exclusivity periods to commercialize Emflaza for the approved indication in the U.S. As the holder of orphan exclusivity, we are required to ensure the availability of sufficient quantities of Emflaza to meet the needs of patients. Failure to do so could result in loss of orphan exclusivity in the U.S.

Translarna for additional indications

Based on its understood mechanism of action, we believe that Translarna may have benefit in the treatment of patients with genetic disorders that arise as a result of a nonsense mutation. We are pursuing studies for Translarna in additional indications including nonsense mutation aniridia, and nonsense mutation Dravet syndrome/CDKL5. We have completed enrollment for our aniridia study and anticipate results during 2019.

Spinal muscular atrophy program

Our spinal muscular atrophy (SMA) collaboration is 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. Currently, our collaboration has three clinical trials ongoing to evaluate the safety and effectiveness of risdiplam (RG7916, RO7034067), the lead compound in the SMA program. Sunfish, a two-part clinical study in pediatric and adult type 2 and type 3 SMA patients initiated in the fourth quarter of 2016, followed by the initiation of Firefish in the fourth quarter of 2016, a two-part clinical study in infants with type 1 SMA. In October 2017, Sunfish transitioned into the pivotal second part of its study, which triggered a $20.0 million milestone payment to us from Roche. In March 2018, Firefish transitioned into the pivotal second part of its study, the primary endpoint of which is the proportion of patients sitting without support after 12 months on risdiplam treatment.

Data from the open label extension of part 1 of the Sunfish trial were presented in October 2018 at the 23rd International Annual Congress of the World Muscle Society, or the World Muscle conference. Risdiplam was well tolerated at all doses and there have been no drug-related safety findings leading to withdrawal. In Sunfish, the data demonstrate that the previously reported median greater than 2-fold SMN protein level increase is maintained over 52 weeks of treatment indicating the durability of the pharmacodynamic effect. Interim clinical data from the Firefish trial were also presented in October 2018 at the World Muscle conference. The median age of first dose was 6.7 months and babies have received risdiplam for a duration of up to 20.3 months. Risdiplam has been well tolerated at all doses and there have been no drug-related safety findings leading to withdrawal. At day 245 of treatment, over 90% of the babies achieved a greater than 4-point increase in CHOP-INTEND score compared to baseline, a rating to evaluate the motor skills of patients with type 1 SMA developed by the Children’s Hospital of Philadelphia. The CHOP-INTEND data were further supported by video footage presented by a principal investigator in the trial, who showed a video of an additional type 1 SMA baby sitting unassisted, bringing the total to 4 babies sitting unassisted as shown in patient videos. Natural history indicates that type 1 SMA babies never achieve this milestone. The video also showed type 1 SMA babies from the FIREFISH trial demonstrating head control and rolling. Moreover, no babies have required a tracheostomy or permanent

ventilation since study initiation and no baby has lost the ability to swallow. Previously published natural history data indicate that in comparable historic cohorts the median age of event-free survival for type 1 SMA infants is between 8 and 10.5 months. In addition, SMN protein level increases of up to 6.5-fold were observed after 28 days of dosing and the increase was sustained.

Jewelfish, an open-label study investigating the safety, tolerability, PK, and PK/pharmacodynamic relationship of risdiplam in type 2 and type 3 SMA patients who have been previously treated with a survival of motor neuron 2 (SMN2)-targeting therapy, initiated in the first quarter of 2017. Preliminary PD data from ten Jewelfish patients presented at the annual meeting of the Academy of American Neurology in April 2018 and at the 22nd Annual SMA Reasercher meeting organized by CureSMA in June 2018 demonstrate increases in SMN2 FL/SMN7 mRNA ratio and SMN protein level increases of up to 4-fold.

Pre-clinical and other programs

We have a pipeline of product candidates that are in early clinical and pre-clinical development. Our pre-clinical and discovery programs are focused on the development of new treatments for multiple therapeutic areas, including rare diseases and oncology.

In September 2018, our IND submission for PTC 299 for the treatment of acute myeloid leukemia, or AML, became effective. We are currently enrolling patients for a phase 1 AML study.

Funding

The success of Translarna, Emflaza, PTC-AADC, Waylivra, Tegsedi and any other product candidates we may develop, depends largely on obtaining and maintaining reimbursement from governments and third-party insurers. Our revenues are primarily generated from sales of Translarna for the treatment of nmDMD in territories where we are permitted to distribute Translarna under our EAP programs and in countries in the EEA where we were able to obtain acceptable commercial pricing and reimbursement terms, and from sales of Emflaza for the treatment of DMD in the United States.

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, October 2014 and April 2018, our initial public offering of common stock in June 2013, private placements of our preferred stock, collaborations, bank debt and convertible debt financings, the Credit Agreement and grants and clinical trial support from governmental and philanthropic organizations and patient advocacy groups in the disease areas addressed by our product candidates. Since 2014, we have also relied on revenue generated from net sales of Translarna for the treatment of nmDMD in territories outside of the United States, and in May 2017, we began to recognize revenue generated from net sales of Emflaza for the treatment of DMD in the United States.

We have a credit and security agreement, or the Credit Agreement, with MidCap Financial Trust, or MidCap Financial, as administrative agent and MidCap Financial and other certain institutions as lenders thereto, that provides for a senior secured term loan facility of $60 million, of which $40 million was drawn by us on May 5, 2017. The remaining $20 million under the senior secured term loan facility would become available to us upon our demonstration (on or prior to December 31, 2018) of net product revenue equaling or exceeding $120 million for the trailing 12 month period. The maturity date of the Credit Agreement is May 1, 2021, unless terminated earlier.

In April 2018, we closed an underwritten public offering of our common stock pursuant to a registration statement on Form S-3. We issued and sold an aggregate of 4,600,000 shares of common stock under the registration statement at a public offering price of $27.04 per share, including 600,000 shares issued upon exercise by the underwriters of their option to purchase additional shares. We received net proceeds of approximately $117.9 million after deducting underwriting discounts and commissions and other offering expenses payable by us.

As of September 30, 2018, we had an accumulated deficit of $890.6 million. We had a net loss of $79.8 million and $80.3 million for the nine month periods ended September 30, 2018 and 2017, respectively.

We anticipate that our expenses will continue to increase in connection with our commercialization efforts in the United States, the EEA, Latin America and other territories, including the expansion of our infrastructure and corresponding 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 Study 041 and our open label extension trials of Translarna for the treatment of nmDMD as well as our studies for nonsense mutation aniridia and nonsense mutation Dravet syndrome/CDKL5 and our FDA post-marketing requirements with respect to Emflaza in the United States. We also expect to incur ongoing research and development expenses for our other product candidates, including our gene therapy and oncology programs. In addition, we may incur substantial costs in connection with our efforts to advance our regulatory submissions. 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. In 2019, we plan to file requests for marketing

authorizations for PTC-AADC with the FDA and EMA and for Tegsedi with ANVISA.These efforts may significantly impact the timing and extent of our commercialization expenses.

We may seek to continue to expand and diversify our product pipeline through opportunistically in-licensing or acquiring the rights to products, product candidates or technologies and we may incur expenses, including with respect to transaction costs, subsequent development costs or any upfront, milestone or other payments or other financial obligations associated with any such transaction, which would increase our future capital requirements.

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. Additionally, under the terms of our Credit Agreement cash interest payments are payable monthly in arrears. 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 including significant legal, accounting, investor relations and other expenses.

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 United States and sales of Emflaza for the treatment of DMD in the United States. 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 SMA with Roche and the SMA Foundation (SMAF) had 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.

In October 2017, we announced that the joint development program in SMA with Roche and SMAF had transitioned into the pivotal second part of its study evaluating the efficacy and safety of RG7916 in pediatric and adult Type 2/3 SMA patients. The achievement of this milestone triggered a $20.0 million payment to us from Roche which we recorded as collaboration revenue at time of achievement.

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 in connection with Study 041 for Translarna for the treatment of nmDMD, our studies of Translarna in nonsense mutation aniridia and nonsense mutation Dravet syndrome/CDKL5, activities under our gene therapy and oncology programs, and performance of our FDA post-marketing requirements with respect to Emflaza in the United States. The timing and amount of these expenses will depend upon the outcome of our 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 products or product candidates and the related expansion of our research and development organization, regulatory requirements, advancement of our preclinical programs, and product 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, 2018 and 2017.

	Three Months Ended September 30,	
	2018	2017
	(in thousands)	
Translarna (nmDMD, nmCF, nmMPS I, aniridia and Dravet)	$ 33,878	$ 20,834
Oncology	3,495	555
Next generation nonsense readthrough	1,653	1,365
Emflaza	4,670	1,859
Other research and preclinical	10,672	5,411
Total research and development	$ 54,368	$ 30,024

	Nine Months Ended September 30,	
	2018	2017
	(in thousands)	
Translarna (nmDMD, nmCF, nmMPS I, aniridia and Dravet)	$ 68,552	$ 61,276
Oncology	8,467	2,735
Next generation nonsense readthrough	4,905	4,145
Emflaza	10,676	4,303
Other research and preclinical	25,737	15,763
Total research and development	$ 118,337	$ 88,222

We discontinued our clinical studies for nonsense mutation cystic fibrosis (nmCF) and nonsense mutation mucopolysaccharidosis type I (nmMPS I) in 2017 and we expect the research and development costs for those programs to continue to decline as we complete the wind down of those programs.

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

- the scope, rate of progress and expense of our clinical trials and other research and development activities;
- the potential benefits of our products and product candidates over other therapies;
- our ability to market, commercialize and achieve market acceptance for any of our products or 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 for our products 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 our products or product candidates could mean a significant change in the costs and timing associated with the development of that product or 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, commercial, 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 and miscellaneous selling costs.

We expect that selling, general and administrative expenses will increase in future periods in connection with our continued efforts to commercialize Emflaza in the United States, our continued efforts to commercialize Translarna for the treatment of nmDMD in territories outside the United States, our efforts to commercialize Waylivra and Tegsedi in Latin America and the Caribbean and to support our operations, 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 and interest expense from the Credit Agreement.

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.

During the three and nine months ended September 30, 2018, there were no material changes to our critical accounting policies as reported in our Annual Report on Form 10-K for the year ended December 31, 2017, which was filed with the Securities and Exchange Commission, or SEC, on March 6, 2018, or the 2017 Annual Report on Form 10-K, other than those disclosed below.

Revenue recognition

Periods prior to January 1, 2018

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

Prior to the second quarter of 2017, our net product sales consisted of sales of Translarna for the treatment of nmDMD in territories outside of the U.S. 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 our third-party partner distributors. Revenue is recognized when risk of ownership has transferred. Our third-party partner 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.

In May 2017, we began the commercialization of Emflaza in the U.S. We recorded product revenue related to the sales of Emflaza in the U.S. in accordance with ASC 605-15, when persuasive evidence of an arrangement exists, delivery has occurred and title of the product and associated risk of loss has passed to the customer, the price is fixed or determinable and collection from the customer has been reasonably assured. Due to the early stage of the product launch, we determined that we were not able to reliably make certain estimates, including returns, necessary to recognize product revenue upon shipment to distributors. As a result, we recorded net product revenue for Emflaza using a deferred revenue recognition model (sell-through). Under the deferred revenue model, we did not recognize revenue until Emflaza was shipped to the specialty pharmacy.

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

We evaluate all contingent consideration earned, such as a milestone payment, using the criteria as provided by ASC 605-28, Revenue Recognition—Milestone Method. At the inception of a collaboration arrangement, we evaluate if a milestone payment is 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 a substantive milestone 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 revenue for reimbursements of research and development costs under collaboration agreements as the services are performed. We record these reimbursements as revenue and not as a reduction of research and development expenses as we have the risks and rewards as the principal in the research and development activities.

Periods commencing January 1, 2018

Our net product revenue consists of sales of Translarna in territories outside of the U.S. and sales of Emflaza in the U.S., both for the treatment of DMD.

Net Product Revenue

We recognize revenue when performance obligations with customers have been satisfied. Our performance obligations are to provide Translarna or Emflaza based on customer orders from distributors, hospitals, specialty pharmacies or retail pharmacies. The performance obligations are satisfied at a point in time when our customer obtains control of either Translarna or Emflaza, which is typically upon delivery. We invoice customers after the products have been delivered and invoice payments are generally due within 30 to 90 days of invoice date. We determine the transaction price based on fixed consideration in its contractual agreements. Contract liabilities arise in certain circumstances when consideration is due for goods not yet provided. As we have identified only one distinct performance obligation, the transaction price is allocated entirely to either product sales of Translarna or Emflaza. In determining the transaction price, a significant financing component does not exist since the timing from when we deliver product to when the customers pay for the product is typically less than one year. Customers in certain countries pay in advance of product delivery. In those instances, payment and delivery typically occur in the same month.

We record product sales net of any variable consideration, which includes discounts, allowances, rebates and distribution fees. We use the expected value or most likely amount method when estimating variable consideration, unless discount or rebate terms are specified within contracts. Historically, returns of Translarna and Emflaza were immaterial to our financial statements. The identified variable consideration is recorded as a reduction of revenue at the time revenues from product sales are recognized. These estimates for variable consideration are adjusted to reflect known changes in factors and may impact such estimates in the quarter those changes are known. Revenue recognized does not include amounts of variable consideration that are constrained.

In relation to customer contracts, we incur costs to fulfill a contract but do not incur costs to obtain a contract. These costs to fulfill a contract do not meet the criteria for capitalization and are expensed as incurred.

Upon adoption of ASC Topic 606 on January 1, 2018, we have elected the following practical expedients:

- Portfolio Approach - We applied the Portfolio Approach to contract reviews within identified revenue streams that have similar characteristics and we believe this approach would not differ materially than if applying ASC Topic 606 to each individual contract.

- Significant Financing Component - We expect the period between when an we transfer a promised good or service to a customer and when the customer pays for the good or service to be one year or less.

- Immaterial Performance Obligations - We disregard promises deemed to be immaterial in the context of the contract.

- Shipping and Handling Activities - We consider any shipping and handling costs that are incurred after the customer has obtained control of the product as a cost to fulfill a promise.

Shipping and handling costs associated with finished goods delivered to customers are recorded as a selling expense.

Collaboration Revenue

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

At the inception of a collaboration arrangement, we need to first evaluate if the arrangement meets the criteria in ASC Topic 808 “Collaborative Arrangements” to then determine if ASC Topic 606 is applicable by considering whether the collaborator meets the definition of a customer. If the criteria are met, we assess the promises in the arrangement to identify distinct performance obligations.

For licenses of intellectual property, we assess, at contract inception, whether the intellectual property is distinct from other performance obligations identified in the arrangement. If the licensing of intellectual property is determined to be distinct, revenue is recognized for nonrefundable, upfront license fees when the license is transferred to the customer and the customer can use and benefit from the license. If the licensing of intellectual property is determined not to be distinct, then the license will be bundled with other promises in the arrangement into one distinct performance obligation. We determine if the bundled performance obligation is satisfied over time or at a point in time. If we conclude that the nonrefundable, upfront license fees will be recognized over time, we assess the appropriate method of measuring proportional performance.

For milestone payments, we assess, at contract inception, whether the development or sales-based milestones are considered probable of being achieved. If it is probable that a significant revenue reversal will occur, we will not record revenue until the uncertainty has been resolved. Milestone payments that are contingent upon regulatory approval are not considered probable of being achieved until the applicable regulatory approvals or other external conditions are obtained as such conditions are not within our control. If it is probable that a significant revenue reversal will not occur, we will estimate the milestone payments using the most likely amount method. We will re-assess the development and sales-based milestones each reporting period to determine the probability of achievement.

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

Inventory and cost of product sales

Inventory

Inventories are stated at the lower of cost and net realizable value with cost determined on a first-in, first-out basis by product. We capitalize inventory costs associated with products following regulatory approval when future commercialization is considered probable and the future economic benefit is expected to be realized. Translarna and Emflaza product which may be used in clinical development programs are included in inventory and charged to research and development expense when the product enters the research and development process and no longer can be used for commercial purposes. Inventory used for marketing efforts are charged to selling, general and administrative expense.

We periodically review inventory for excess amounts or obsolescence and write down obsolete or otherwise unmarketable inventory to its estimated net realizable value. We recorded a $1.6 million writedown of inventory for the three month period ended September 30, 2018 primarily related to inventory labeling changes. Additionally, though our products are subject to strict quality control and monitoring which is performed throughout the manufacturing processes, certain batches or units of product may not meet quality specifications resulting in a charge to cost of product sales.

Cost of product sales

Cost of product sales consists of the cost of inventory sold, manufacturing and supply chain costs, storage costs, amortization of the acquired intangible asset and royalty payments associated with net product sales.

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.

Indefinite-lived intangible assets

Indefinite-lived intangible assets consist of in-process research and development (IPR&D). IPR&D acquired directly in a transaction other than a business combination is capitalized if the projects will be further developed or have an alternative future use; otherwise they are expensed. The fair values of IPR&D projects acquired in business combinations are capitalized. Several methods may be used to determine the estimated fair value of the IPR&D acquired in a business combination. We utilize the "income method", and use estimated future net cash flows that are derived from projected sales revenues and estimated costs. These projections are based on factors such as relevant market size, patent protection, and expected pricing and industry trends. The estimated future net cash flows are then discounted to the present value using an appropriate discount rate. These assets are treated as indefinite-lived intangible assets until completion or abandonment of the projects, at which time the assets are amortized over the remaining useful life or written off, as appropriate. IPR&D intangible assets that are determined to have had a drop in their fair value are adjusted downward and an impairment is recognized in the statement of operations. These assets are tested at least annually or sooner when a triggering event occurs that could indicate a potential impairment.

Goodwill

Goodwill represents the amount of consideration paid in excess of the fair value of net assets acquired as a result of our business acquisitions accounted for using the acquisition method of accounting. Goodwill is not amortized and is subject to impairment testing on an annual basis or when a triggering event occurs that may indicate the carrying value of the goodwill is impaired.

Results of operations

Three months ended September 30, 2018 compared to three months ended September 30, 2017

The following table summarizes revenues and selected expense and other income data for the three months ended September 30, 2018 and 2017.

	Three Months Ended September 30,		Change 2018 vs. 2017
(in thousands)	2018	2017	
Net product revenue	$ 53,021	$ 41,780	$ 11,241
Collaboration and grant revenue	570	73	497
Cost of product sales, excluding amortization of acquired intangible asset	3,292	1,582	1,710
Amortization of acquired intangible asset	5,793	9,716	(3,923)
Research and development expense	54,368	30,024	24,344
Selling, general and administrative expense	38,368	31,423	6,945
Interest expense, net	(3,118)	(3,421)	303
Other income, net	734	766	(32)
Income tax expense	(355)	(191)	(164)

Net product revenues. Net product revenues were $53.0 million for the three months ended September 30, 2018, an increase of $11.2 million, or 27%, from $41.8 million for the three months ended September 30, 2017. The increase in net product revenue was primarily due to the increase in revenue of Emflaza in the United States, which launched in May 2017.

Collaboration and grant revenues. Collaboration and grant revenues were $0.6 million for the three months ended September 30, 2018 and $0.1 million for the three months ended September 30, 2017. Revenues are from ongoing collaboration arrangements.

Cost of product sales, excluding amortization of acquired intangible asset. Cost of product sales, excluding amortization of acquired intangible asset, were $3.3 million for the three months ended September 30, 2018 and $1.6 million for the three months ended September 30, 2017. Cost of product sales, excluding amortization of acquired intangible asset, consist primarily of royalty payments associated with Emflaza and Translarna net product sales and costs associated with Emflaza and Translarna product sold during the period. For Translarna sold in 2017, the majority of related manufacturing costs incurred had previously been expensed prior to January 1, 2017 as research and development expenses.

Amortization of acquired intangible asset. Amortization of the acquired intangible asset was $5.8 million for the three months ended September 30, 2018 and $9.7 million for the three months ended September 30, 2017, resulting from the acquisition of all rights to Emflaza. The amount allocated to the Emflaza intangible asset will be amortized on a straight-line basis over its estimated useful life of approximately seven years from the date of the completion of our acquisition of all rights to Emflaza, the period of estimated future cash flows.

Research and development expense. Research and development expense was $54.4 million for the three months ended September 30, 2018, an increase of $24.3 million, or 81%, from $30.0 million for the three months ended September 30, 2017. The increase was primarily due to increased investment in research programs and the advancement of the clinical pipeline, as well as the Akcea upfront licensing fee of $12.0 million paid during the current quarter.

Selling, general and administrative expense. Selling, general and administrative expense was $38.4 million for the three months ended September 30, 2018, an increase of $6.9 million, or 22%, from $31.4 million for the three months ended September 30, 2017. The increase resulted primarily from the continued investment in commercial activities for Emflaza, which launched in May 2017, and Translarna, as well as $1.5 million in Agilis acquisition related expenses.

Interest expense, net. Interest expense, net was $3.1 million for the three months ended September 30, 2018, a decrease of $0.3 million, or 9%, from $3.4 million for the three months ended September 30, 2017. The decrease in interest expense, net was primarily due to increased interest income from investments, which partially offset current year interest expense recorded from the Convertible Notes and the Credit Agreement.

Other income, net. Other income, net was $0.7 million for the three months ended September 30, 2018, a decrease in income of $0.03 million, or 4%, from other income, net of $0.8 million for the three months ended September 30, 2017. The decrease in other income, net resulted primarily from exchange rate changes in the current period.

Income tax expense. Income tax expense was $0.4 million for the three months ended September 30, 2018 and $0.2 million for the three months ended September 30, 2017. 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 three months ended September 30, 2018 differed from the amounts computed by applying the U.S. federal income tax rate of 21% to loss before tax expense as a result of a favorable change in the jurisdictional mix of profits in 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, 2018 compared to nine months ended September 30, 2017

The following table summarizes revenues and selected expense and other income data for the nine months ended September 30, 2018 and 2017.

(in thousands)	Nine Months Ended September 30, 2018	2017	Change 2018 vs. 2017
Net product revenue	$ 177,172	$ 116,113	$ 61,059
Collaboration and grant revenue	1,224	249	975
Cost of product sales, excluding amortization of acquired intangible asset	8,909	2,142	6,767
Amortization of acquired intangible asset	16,815	9,952	6,863
Research and development expense	118,337	88,222	30,115
Selling, general and administrative expense	104,882	85,788	19,094
Interest expense, net	(9,306)	(8,648)	(658)
Other income (expense), net	1,066	(1,373)	2,439
Income tax expense	(964)	(507)	(457)

Net product revenues. Net product revenues were $177.2 million for the nine months ended September 30, 2018, an increase of $61.1 million, or 53%, from $116.1 million for the nine months ended September 30, 2017. The increase in net product revenue was primarily due to the increase in net product revenue in existing markets where Translarna is available as well as continued geographic expansion into new territories, in addition to net product revenue of Emflaza in the United States, which launched in May 2017.

Collaboration and grant revenues. Collaboration and grant revenues were $1.2 million for the nine months ended September 30, 2018, an increase of $1.0 million, or 392%, from $0.2 million for the nine months ended September 30, 2017. These revenues are from ongoing collaboration arrangements.

Cost of product sales, excluding amortization of acquired intangible asset. Cost of product sales, excluding amortization of acquired intangible asset, were $8.9 million for the nine months ended September 30, 2018 and $2.1 million for the nine months ended September 30, 2017. Cost of product sales, excluding amortization of acquired intangible asset, consist primarily of royalty payments associated with Emflaza and Translarna net product sales and costs associated with Emflaza and Translarna product sold during the period. For Translarna sold in 2017, the majority of related manufacturing costs incurred had previously been expensed prior to January 1, 2017 as research and development expenses.

Amortization of acquired intangible asset. Amortization of the acquired intangible asset was $16.8 million for the nine months ended September 30, 2018 and $10.0 million for the nine months ended September 30, 2017, resulting from the acquisition of Emflaza. The amount allocated to the Emflaza intangible asset will be amortized on a straight-line basis over its estimated useful life of approximately seven years from the date of the completion of our acquisition of all rights to Emflaza, the period of estimated future cash flows.

Research and development expense. Research and development expense was $118.3 million for the nine months ended September 30, 2018, an increase of $30.1 million, or 34%, from $88.2 million for the nine months ended September 30, 2017. The increase was primarily due to increased investment in research programs and the advancement of the clinical pipeline, as well as the Akcea upfront licensing fee of $12.0 million paid during the current period.

Selling, general and administrative expense. Selling, general and administrative expense was $104.9 million for the nine months ended September 30, 2018, an increase of $19.1 million, or 22%, from $85.8 million for the nine months ended September 30, 2017. The increase resulted primarily from the continued investment in commercial activities for Emflaza, which launched in May 2017, and Translarna, as well as $1.5 million in Agilis acquisition related expenses.

Interest expense, net. Interest expense, net was $9.3 million for the nine months ended September 30, 2018, an increase in expense of $0.7 million, or 8%, from interest expense of $8.6 million for the nine months ended September 30, 2017. The increase in interest expense was primarily due to current year interest expense recorded from the Convertible Notes and the Credit Agreement, partially offset by interest income from investments.

Other income (expense), net. Other income, net was $1.1 million for the nine months ended September 30, 2018, and other expense, net was $1.4 million for nine months ended September 30, 2017. The change in other income (expense), net was primarily from foreign currency fluctuations in exchange rates in the current period.

Income tax expense. Income tax expense was $1.0 million for the nine months ended September 30, 2018 and $0.5 million for the nine months ended September 30, 2017. 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, 2018 differed from the amounts computed by applying the U.S. federal income tax rate of 21% to loss before tax expense as a result of a favorable change in the jurisdictional mix of profits in 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 and Emflaza for the treatment of DMD while also devoting a substantial portion of our efforts on research and development programs related to Translarna, gene therapy, and our other product candidates. To date, almost all of our product revenue has been attributable to sales of Translarna for the treatment of nmDMD in territories outside of the United States. Since May 2017, we have also begun to generate product revenue from Emflaza for the treatment of DMD in the United States. Our ongoing ability to generate revenue from sales of Translarna for the treatment of nmDMD is dependent upon our ability to maintain our marketing authorization in the EEA and secure market access through commercial programs following the conclusion of pricing and reimbursement terms at sustainable levels in the member states of the EEA or through EAP programs in the EEA and other territories. The marketing authorization requires annual review and renewal by the European Commission following reassessment by the EMA of the benefit-risk balance of the authorization and is subject to the specific obligation to conduct Study 041. Our ability to generate product revenue from Emflaza will largely depend on the coverage and reimbursement levels set by governmental authorities, private health insurers and other third-party payors.

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, the Credit Agreement and grants and clinical trial support from governmental and philanthropic organizations and patient advocacy groups in the disease areas addressed by our product candidates. Since 2014, we have also relied on revenues generated from net sales of Translarna for the treatment of nmDMD in territories outside of the United States, and in May 2017, we began to recognize revenue generated from net sales of Emflaza for the treatment of DMD in the United States. Based on our current commercial, research and development plans, we expect to continue to incur significant operating expenses for the foreseeable future, which we anticipate will be partially offset by revenues generated from the sale of both Translarna and Emflaza, as well as Waylivra and Tegsedi once our commercialization efforts of them commence. As a result, while we expect to continue to generate operating losses in 2018, we anticipate that operating losses generated in future periods should decline versus prior periods. 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 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.

On May 5, 2017, we entered into the Credit Agreement with MidCap Financial, which provides for a senior secured term loan facility of $60 million, of which $40 million was drawn by us on May 5, 2017. The remaining $20 million under the senior secured term loan facility would become available to us upon our demonstration (on or prior to December 31, 2018) of net product revenue equaling or exceeding $120 million for the trailing 12 month period. The maturity date of the Credit Agreement is May 1, 2021, unless terminated earlier. The facility is structured to require only monthly interest payments for the initial two years with principal amortization beginning in years three and four. The facility bears interest at a rate per annum equal to LIBOR (with a LIBOR floor rate of 1.00%) plus 6.15%, as well as additional upfront and administrative fees and expenses.

In April 2018, we closed an underwritten public offering of 4,600,000 shares of common stock under the registration statement at a public offering price of $27.04 per share, including 600,000 shares issued upon exercise by the underwriters of their option to purchase additional shares. We received net proceeds of approximately $117.9 million after deducting underwriting discounts and commissions and other offering expenses payable by us.

Cash flows

As of September 30, 2018, we had cash, cash equivalents and marketable securities of $249.4 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)	**2018**	**2017**
Cash provided by (used in):		
Operating activities	(12,498)	(31,351)
Investing activities	(18,017)	67,159
Financing activities	127,845	42,367

Net cash used in operating activities was $12.5 million for the nine months ended September 30, 2018 and $31.4 million for the nine months ended September 30, 2017. The net cash used in operating activities primarily relates to supporting clinical development and commercial activities, partially offset by increased cash receipts resulting from higher net product revenues.

Net cash used in investing activities was $18.0 million for the nine months ended September 30, 2018 and net cash provided by investing activities was $67.2 million for the nine months ended September 30, 2017. Cash used in investing activities for the nine months ended September 30, 2018 was primarily related to the acquisition of Agilis and royalty payments related to Emflaza product rights, partially offset by the net redemption of marketable securities. Cash provided by investing activities for the nine months ended September 30, 2017 was primarily related to the net redemption of marketable securities, partially offset by acquisition costs associated with the Emflaza asset acquisition.

Net cash provided by financing activities was $127.8 million for the nine months ended September 30, 2018 and $42.4 million for the nine months ended September 30, 2017. Cash provided by financing activities for the nine months ended September 30, 2018 is primarily attributable to the April 2018 equity offering and the exercise of options and issuance of stock under the ESPP. Cash provided by financing activities for the nine months ended September 30, 2017 is primarily attributable to borrowings under the Credit Agreement and the exercise of options and issuance of stock under the ESPP.

Funding requirements

We anticipate that our expenses will increase in connection with our commercialization efforts in the United States, the EEA, Latin America and other territories, including expansion of our infrastructure and corresponding 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 Study 041 and our open label extension trials of Translarna for the treatment of nmDMD as well as our studies for nonsense mutation aniridia and nonsense mutation Dravet syndrome/CDKL5 and our FDA post-marketing requirements with respect to Emflaza in the United States. We also expect to incur ongoing research and development expenses for our other product candidates, including our gene therapy and oncology program. In addition, we may incur substantial costs in connection with our efforts to advance our regulatory submissions. 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. In 2019, we plan to file requests for marketing authorizations for PTC-AADC with the FDA and EMA and for Tegsedi with ANVISA. These efforts may significantly impact the timing and extent of our commercialization expenses.

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

- seek to integrate Agilis's operations and employees into our business and seek to satisfy contractual and regulatory obligations we assumed in connection with the Agilis acquisition;
- seek to satisfy contractual and regulatory obligations in conjunction with the Akcea Agreement, including the potential commercialization of Tegsedi and Waylivra in the PTC Territory;
- execute our strategy for Emflaza in the United States, including commercialization and integration efforts;
- satisfy contractual and regulatory obligations that we assumed through the Emflaza acquisition;
- are required to complete any additional clinical trials, non-clinical studies or CMC assessments or analyses in order to advance Translarna for the treatment of nmDMD in the United States or elsewhere;

- are required to take other steps, in addition to Study 041, to maintain our current marketing authorization in the EEA for Translarna for the treatment of nmDMD or to obtain further marketing authorizations for Translarna for the treatment of nmDMD or other indications in the EEA or elsewhere;
- initiate or continue the research and development of Translarna for additional indications and of our other product candidates, including for our gene therapy and oncology programs;
- seek to discover and develop additional product candidates;
- seek to expand and diversify our product pipeline through strategic transactions;
- 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 term loan facility with MidCap Financial, 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:

- our ability to commercialize and market Tegsedi and Waylivra in the PTC Territory;
- our ability to commercialize and market Emflaza for the treatment of DMD in the United States;
- our ability to negotiate, secure and maintain adequate pricing, coverage and reimbursement terms, on a timely basis, with third-party payors for Emflaza for the treatment of DMD in the United States and for Translarna for the treatment of nmDMD in the EEA and other territories outside of the United States;
- our ability to maintain orphan exclusivity for, and successfully complete all FDA post-marketing requirements with respect to, Emflaza, or to obtain an additional six-month period of pediatric exclusivity;
- our ability to maintain the marketing authorization in the EEA for Translarna for the treatment of nmDMD, including whether the EMA determines on an annual basis that the benefit-risk balance of Translarna supports renewal of our marketing authorization in the EEA, on the current approved label;
- the costs, timing and outcome of Study 041;
- the costs, timing and outcome of our efforts to advance Translarna for the treatment of nmDMD in the United States, including, whether we will be required to perform additional clinical trials, non-clinical studies or CMC assessments 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 United States;
- the progress and results of our open label extension clinical trials of Translarna for the treatment of nmDMD as well as our studies for nonsense mutation aniridia and nonsense mutation Dravet syndrome/CDKL5 and activities under our gene therapy and oncology programs;
- the scope, costs and timing of our commercialization activities, including product sales, marketing, legal, regulatory, distribution and manufacturing, for both Emflaza for the treatment of DMD and Translarna for the treatment of nmDMD, for Tegsedi, for Waylivra and for 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, including those in our gene therapy and oncology programs, and Translarna in other territories or for indications other than nmDMD;
- our ability to satisfy our obligations under the terms of the Credit Agreement with MidCap Financial;
- 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, including those in our gene therapy and oncology programs;

- revenue received from commercial sales of Translarna, Emflaza, Tegsedi, Waylivra, or any of our other product candidates;
- 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;
- 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, product candidates, and technologies, including the success of any acquisition, in-licensing or other strategic transaction we may pursue, and the costs of subsequent development requirements and commercialization efforts, including with respect to our acquisition of Emflaza, our acquisition of Agilis, and our licensing of Tegsedi and Waylivra; 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.

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, 2018, 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, 2017, other than as disclosed below.

(in thousands)	Total	Less than 1 year	1 - 3 years	4 - 5 years	More than 5 years
Deferred consideration payable (1)	$ 40,000		40,000	—	—

(1) Pursuant to the Merger Agreement with Agilis, we are required to pay $40.0 million of development milestone payments, or deferred consideration payments, no later than the second anniversary of the closing of the Merger, regardless of

whether the applicable milestones have been achieved. The payment schedule above reflects our expected timing of when the payments will be made as of September 30, 2018. The fair value of the deferred consideration payments at the acquisition date was estimated to be $38.2 million.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

During the period ended September 30, 2018, 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, 2017.

Item 4. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and our Principal Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of September 30, 2018. 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, 2018, our Chief Executive Officer and Principal 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, 2018 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 former Chief Financial Officer. The lawsuits were consolidated into one action captioned *In re PTC Therapeutics, Inc. Securities Litigation*, No. 16-1224 (KM) (the "Securities Class Action"). A consolidated amended complaint was filed on January 13, 2017. The complaint alleged 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 sought, among other things, compensatory damages for purchasers of the Company's common stock between November 6, 2014 and February 23, 2016, as well as attorneys' fees and costs. On February 14, 2017, the defendants filed a motion to dismiss the consolidated amended complaint. On August 28, 2017, the motion to dismiss was granted in part and denied in part. On September 25, 2017, defendants filed an answer and affirmative defenses to the consolidated amended complaint. On January 10, 2018, the parties agreed to a settlement in principle of all legal claims, subject to court approval, funded by the Company's insurance subject to the applicable deductible. The Court approved the settlement and dismissed the case on September 10, 2018.

On September 19, 2017, a purported stockholder of the Company filed a derivative lawsuit in the United States District Court for the District of New Jersey against our Chief Executive Officer, our former Chief Financial Officer, and current or former directors (Michael Schmertzler; Richard Aldrich; Allan Jacobson; Adam Koppel; Michael Kranda; C. Geoffrey McDonough; Ronald C. Renaud, Jr.; David P. Southwell; Jerome Zeldis; and Glenn D. Steele, Jr.), with the caption *Choi v. Peltz, et al.*, No. 17-cv-07216. The Company was named as a nominal defendant. On October 10, 2017, another purported stockholder of the Company filed a derivative lawsuit in the United States District Court for the District of New Jersey against the same defendants and nominal defendant, with the caption *Kim v. Peltz, et al.*, No. 17-cv-08062. On January 17, 2018, a third purported stockholder of the Company filed a derivative lawsuit in the United States District Court for the District of New Jersey against the same defendants and nominal defendant, with the caption *Lee v. Peltz, et al.*, No. 2:18-cv-00730. The *Choi*, *Kim* and *Lee* actions were consolidated and captioned *In re PTC Therapeutics, Inc. Derivative Litigation*, No. 17-cv-07216 (the "Consolidated Derivative Action"). The Consolidated Derivative Action alleged violations of Section 14(a) of the Securities Exchange Act of 1934, breaches of defendants' fiduciary duties, unjust enrichment, abuse of control, and gross mismanagement based on allegations that defendants made or approved improper statements regarding the NDA for Translarna for the treatment of nmDMD that the Company submitted to the FDA in December 2015. The Consolidated Derivative Action sought, among other things, any damages sustained by the Company as a result of the defendants' alleged wrongdoing (including fees associated with the Securities Class Action), an order directing the Company to take all necessary actions to reform and improve its corporate governance and internal procedures, restitution from the defendants, and attorneys' fees and costs. On February 12, 2018, the defendants moved to dismiss the Consolidated Derivative Action. On March 20, 2018, the parties agreed to a settlement in principle of all legal claims, comprising payment of plaintiffs' attorneys' fees and certain corporate governance reforms. The Court approved the settlement and dismissed the case on July 27, 2018.

Item 1A. Risk Factors

We have set forth in Item 1A to our Annual Report on Form 10-K for the year ended December 31, 2017, risk factors relating to our business, our industry, our structure and our common stock. Readers of this Quarterly Report on Form 10-Q are referred to such Item 1A for a more complete understanding of risks concerning us. There have been no material changes in our risk factors since those published in such Form 10-K for the year ended December 31, 2017, other than as reported in Item Part II Item 1A on our Form 10-Q for the periods ended March 31, 2018 and June 30, 2018, and in Exhibit 99.2 to our Current Report on Form 8-K filed on August 24, 2018.

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

Recent Sales of Unregistered Securities

Inducement grant awards. Pursuant to the Nasdaq inducement grant exception, during the quarter ended September 30, 2018, we issued options to purchase an aggregate of 653,900 shares of common stock to certain new hire employees at a weighted-average exercise price of $43.36 per share. The shares underlying these options will be registered on a Form S-8 registration statement prior to the first vesting event applicable to each such award.

Item 6. Exhibits.

Exhibit Number	Description of Exhibit
2.1†	Agreement and Plan of Merger, dated July 19, 2018, by and among PTC Therapeutics, Inc., Agility Merger Sub, Inc., Agilis Biotherapeutics, Inc., and solely in its capacity as equityholder representative, Shareholder Representative Services LLC (incorporated by reference to Exhibit 2.1 to the Current Report on Form 8-K filed by the Registrant on July 19, 2018)
10.1	Bridge Loan and Security Agreement, dated as July 19, 2018, by and among PTC Therapeutics, Inc., Agilis Biotherapeutics, Inc., and the Guarantors as defined therein (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed by the Registrant on July 19, 2018)
10.2	Amendment No. 1 and Limited Consent to Credit and Security Agreement, dated as of July 19, 2018, by and among PTC Therapeutics, Inc., MidCap Financial trust and the Lenders as defined therein (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K filed by the Registrant on July 19, 2018)
10.3††	Collaborative Research Agreement, dated September 30, 2015, as amended, by and between National Taiwan University and Agilis Biotherapeutics, Inc. (formerly Agilis Biotherapeutics, LLC)
10.4††	License and Technolgy Transfer Agreement, dated December 23, 2015, by and between National Taiwan University and Agilis Biotherapeutics, Inc. (formerly Agilis Biotherapeutics, LLC)
10.5††	Collaboration and License Agreement, dated August 1, 2018, by and between PTC Therapeutics International Limited and Akcea Therapeutics, Inc.
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*

† Confidential treatment has been granted for certain portions that are omitted from this exhibit. The omitted information has been filed separately with the U.S. Securities and Exchange Commission (the "SEC") pursuant to the registrant's application for confidential treatment. In addition, schedules have been omitted from this exhibit pursuant to Item 601(b)(2) of Regulation S-K. A copy of any omitted schedule will be furnished supplementally to the SEC upon request; provided, however, that the registrant may request confidential treatment for any document so furnished.

†† Confidential treatment has been requested for certain portions that are omitted from this exhibit. The omitted information has been filed separately with the U.S. Securities and Exchange Commission (the "SEC") pursuant to the registrant's application for confidential treatment.

* Submitted electronically herewith.

In accordance with SEC Release 33-8238, Exhibits 32.1 and 32.2 are being furnished and not filed.

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 5, 2018

By: /s/ Christine Utter

Christine Utter

Principal Financial Officer

(Principal Financial and Accounting Officer and Duly Authorized Signatory)

Confidential Materials omitted and filed separately with the
Securities and Exchange Commission. Double asterisks denote omissions.

Exhibit 10.3

Collaborative Research Agreement

This Collaborative Research Agreement ("Agreement") is made and entered into this 30th day of September, 2015 (the "Commencement Date") by and between National Taiwan University at No. 1, Sec. 4, Roosevelt Road, Taipei, 10617 Taiwan (R.O.C) (hereinafter "NTU") and Agilis Biotherapeutics, LLC, a Delaware limited liability company duly organized under law and having an address at 245 First St, Suite 1800, Cambridge, MA, 02142 USA (hereinafter "COMPANY"). The Parties do hereby mutually agree the terms and conditions set forth below.

1 Mutual Covenant

COMPANY hereby agrees to consign NTU and its designated investigator Dr. Wuh-Liang (Paul) Hwu ("Principal Investigator") to carry out a certain Project (hereinafter referred to as "the Project"), and NTU agrees to use commercially reasonable efforts to perform the Project as defined in Annex 1, which is incorporated into this Agreement and made a part hereof.

2Term of the Research

This Project shall be carried out starting from September 30, 2015, ("Effective Date") and remain in effect until September 30, 2017 (the "Term").

3Research Cost and Payment

3.1 It is agreed to and understood by the parties that NTU shall be paid for the Project and the amount shall be US$[**] (hereinafter "Research Cost"). [**] percent ([**]%) of Research Cost (US$[**]) is for executing the research outlined in Annex 1, and [**] percent ([**]%) of Research Cost (US$[**]) is for NTU's overheads. Additionally, Agilis shall support [**].

3.2 The Research Cost shall be paid by following installment:

3.2.1 US$ [**] shall be payable within [**] after the Effective Date of this Agreement.

3.2.2 US$[**] shall be payable [**] within [**] upon reaching milestones [**].

3.2.3 US$ [**] shall be payable within [**] after [**].

3.3 Unless otherwise explicitly stated in this Agreement, The COMPANY grants the Principal Investigator the right to make all decisions on the usage of Research Cost including but not limited to Principal Investigator's personal cost, staff, consumables, equipment, testing, and other costs towards successful execution of the Project, provided the COMPANY is informed of the decision to be made by the Principal Investigator and the decisions do not affect the focus or objectives of the Project as outlined in Annex 1 or the clinical study protocol outlined in Annex 2.

4Dispense of Payment

The COMPANY will dispense payment according to this Agreement and NTU will confirm receipt of each payment via email.

5 Extension of Term

After COMPANY'S written approval, the Term may be automatically extended for a maximum of one (1) year for one time. NTU shall not request COMPANY to compensate any costs arising from the extension of Term.

6 Progress of Research

COMPANY shall be entitled to request NTU or Principal Investigator, if necessary, to present oral presentation with relevant information according to its progress. COMPANY shall be entitled to designate certain representatives and dispatch them to NTU's premises to inspect the condition of the execution of the research, including data and clinical trial forms and reports. In this regard, NTU and the Principal Investigator shall provide relevant assistance in due course. The COMPANY will be responsible for all expenses related to, but not limited to, airfare, traveling and accommodation.

7NTU owns the facilities purchased by NTU with the payment from COMPANY. NTU may enroll the facilities as national property and manage in compliance with National Property Act.

8Intellectual Property Rights

8.1 Any patent rights, copyrights, rights in circuit layouts and other intellectual property rights of the research result developed or potentially obtained by NTU pursuant to this Agreement and the Principal Investigator (herein after as "Research Result") shall be solely owned by NTU.

8.2 COMPANY shall not apply for registrations of the aforesaid patent rights, copyrights, rights in circuit layouts and other intellectual property rights with the government authorities, unless with NTU's consent or with NTU's abandonment of the right to register.

8.3 NTU shall bear the expense incurred by such applications for registrations, while Company shall provide all requisite assistance to obtain the aforesaid rights.

8.4 NTU hereby grants the Company a Right of First Refusal for an Exclusive, Royalty-bearing License in all territories of the world, which shall be in effect for the entire Term, including any extensions under Section 5 of this Agreement. After the end of the Term as defined in Sections 2 and 5 of this Agreement, the COMPANY shall have [**] from written notice from NTU to accept or decline the Exclusive, Royalty-bearing License. If the COMPANY chooses to decline the Exclusive, Royalty-bearing License, NTU is free to license the Research Result to other parties without any obligation to the COMPANY. COMPANY may choose to accept the Exclusive, Royalty-bearing License at any time during the Term of this Agreement including any extensions under Section 5 of this Agreement. If the COMPANY chooses to accept the Exclusive, Royalty-bearing License, the parties shall negotiate in good faith for a period of up to [**] to reach agreement on the terms of the Exclusive, Royalty-bearing License; and the terms of the Exclusive, Royalty-bearing License provided for under the Right of First Refusal shall include the following:

8.4.1 Territory: All countries of the World

8.4.2 Field: All fields

8.4.3 License Term: 20 years

8.4.4 Licensed Technology: All intellectual property (including patents and patent applications), data, CMC records, documents, materials and know-how pertaining to the AADC gene therapy product and otherwise relating to the Research Results,

8.4.5 Royalty: A royalty-bearing license based on Net Sales of the AADC gene therapy product in the Territory. The Royalty on Net Sales shall be [**] percent ([**]%).

8.4.6 Up-front payments, milestone payments and funding for Phase III (or pivotal trial).

8.4.6.1 Upon signing the Exclusive, Royalty-bearing License, Company shall pay NTU and up-front fee of US$[**]. In addition, upon signing the Exclusive, Royalty-bearing License, Agilis shall commit to funding the proposed Phase III clinical study in AADC deficiency using the Technology of an estimated [**] subjects. The study will be conducted at least in part in Taiwan; however, for purposes of enabling registration in other territories, the Phase III clinical study may also be conducted in other countries as well.

8.4.6.2 Upon [**], Company shall pay NTU a milestone fee of US$[**].

8.4.6.3 Upon [**], Company shall pay NTU a milestone fee of US$[**].

8.4.6.4 Upon [**], Company shall pay NTU US$[**].

8.4.6.5 Milestones: NTU and Principal Investigator shall conduct the Project in accordance with Annex 1, wherein specific Milestones are noted.

8.4.7 License Maintenance Fee. Beginning on the first anniversary of the Effective Date of the Exclusive Royalty-bearing License and for each anniversary thereafter, Company will pay NTU the following annual maintenance fees:

8.4.7.1 US$[**] on the [**] anniversaries;

8.4.7.2 US$[**] on the [**] anniversaries;

8.4.7.3 US$[**] on the [**] anniversaries; and

8.4.7.4 US$[**] for the [**] and each anniversary thereafter until the 20th anniversary.

8.4.7.5 Yearly maintenance fees are nonrefundable, but are creditable against royalties payable.

8.4.8 Royalty and Maintenance Fee Term. The Maintenance Fees noted in Section 8.4.7 and the Royalty noted in Section 8.4.5 shall be in effect for a period of 20 years from the date of execution of the Exclusive, Royalty-bearing License.

8.4.9 Sub-licenses: The Company shall have the right to grant sublicenses through all tiers. In the event Agilis is paid any sub-licensing fee, Agilis shall pay NTU [**]% of any up-front fee and [**]% of any milestone fee, but that fees paid to Agilis for R&D shall not be subject to the sub-licensing fees.

8.4.10 Patents: The Parties shall define responsibilities for prosecuting and maintaining patents and patent applications, if any.

9Result of Research

9.1 NTU and the Principal Investigator shall submit the result of research according to stipulated schedule specified in Project, or proceed accordingly with the following steps if there is no requirement in Project.

9.1.1 NTU and the Principal Investigator shall submit to COMPANY two copies of the mid-term report of the research within [**] from the Effective Date of the Term as specified in article 2.

9.1.2 NTU and the Principal Investigator shall submit to COMPANY two copies of a final report of the research result within [**] after the Term of the research expires as specified in article 2.

10Termination and Force Majeure

10.1 In the event either party fails to materially comply with this Agreement or breaches any article of this Agreement, the other party shall give such party thirty (30) days for remedy with a written notice. If such party fails to correct its own default within thirty (30) days, the non-default party shall be entitled to terminate this Agreement by a respective written notice.

10.2 Termination by Company. Company may terminate this Agreement upon 60 days written notice, if NTU has committed the following breaches and failed to cure the breaches within [**] following written notice by Company to NTU:

10.2.1 NTU fails to execute its responsibility stated in Annex 1, 2, 3 and 4;

10.3 Termination by NTU. NTU may terminate this Agreement upon 60 days prior written notice, if Company has committed the following breaches and failed to cure the breaches within [**] following written notice by NTU to Company:

10.3.1 Company is delinquent on any report or payment;

10.3.2 Company is not diligently developing and commercializing Licensed Product in accordance with agreed upon milestones;

10.3.3 Company is in material breach of any provision; or

10.3.4 Company provides any false report and has failed to correct any inaccuracies in such report.

10.4 Upon the termination at COMPANY'S option, NTU shall return the payment which has not been consumed in the Project to COMPANY without accrued interest. The COMPANY will pay any related additional non-cancellable costs NTU incurred as of the date of termination by COMPANY. The COMPANY may suspend any further payment henceforth.

10.5 In the event that the performance of any obligation under this Agreement by a party is prevented due to acts of God, governmental acts or decisions to act or not to act, wars, hostilities, blockades, civil disturbances, revolutions, strikes, lockouts, fire, typhoons, tidal waves, flood or any other causes beyond the reasonable control of such party, such party shall not be responsible to the other party for failure or delay of performance of its obligations under this Agreement.

11Warranty

11.1 NTU shall be relieved from any warranties including but not limited to the availability or merchantability of the Research Result unless otherwise expressly specified in this Agreement.

11.2 NTU and the Principal Investigator warrants that any information and/or documents related to the Research Project are developed by itself, and warrant that the Project will be conducted in accordance with Annex 1.

12Indemnity of Infringement

12.1 Both parties agree to defend any claims or suits brought against COMPANY based upon a claim that any of the products produced based on the invention of this Agreement and made by COMPANY infringe any patent, copyright, mask work or other intellectual property right. COMPANY shall promptly notify NTU of any such claims and shall provide reasonable and sufficient assistance in connection with defending such claim to secure mutual benefits. NTU shall not be held responsible for any tort against COMPANY or any third party in connection with such infringement. Should COMPANY be involved in such a suit, NTU shall provide all information, documents and materials available for the defense.

12.2 If any patent rights, copyrights, rights in circuit layouts and any other intellectual rights developed by this Research Project are infringed, COMPANY shall immediately notify NTU when asserting its own rights or bringing proper claims or actions against the infringing party. NTU and the Principal Investigator shall assist COMPANY to undergo all necessary procedures or litigation to protect the relevant intellectual property rights to secure the mutual benefits.

13Confidentiality

Any information related to the Research Result and the terms of this Agreement itself will be considered Confidential Information. COMPANY agrees not to disclose to any third parties any and all confidential information without prior written approval from NTU. COMPANY shall demand all members involved in this Research Project comply with this provision in safeguarding the confidential information. Any party or any member involved in this Research Project found to breach this clause shall, at its own expenses, indemnify any and all damages sustained and costs incurred arising from the breach of this confidentiality obligation.

14Non-Competition Clause

The Principal Investigator may not be employed or retained by any third party during the Research Term to get involved with any work whose approach is substantially the same as this Research Project at stated in Annex 1, 2, 3 and 4. Mutual consent between the Principal Investigator and the COMPANY shall be reached to resolve any related issue that may arise.

15Assignment of Rights and Obligations

Neither party shall not assign or transfer any of its rights or obligations contemplated herein to any third party without the prior written consent of the other party, provided

however, that the Company shall be entitled to assign or transfer any of its rights or obligations hereunder to a third party in connection with a merger, acquisition, other business combination or the Company's sale of all or substantially all of its securities or assets.

16Modification of Research Project

This Agreement shall be subject to change or modification by mutual agreement if and when necessary, however, the development and expense of the Research Project shall be adjusted upon the Parties' agreement. If no such agreement is available, either party may terminate this Agreement by a written notice to the other party without incurring any damages arising from such termination. Under such circumstance, COMPANY shall not request from NTU reimbursement of the money already consumed in the Research Project, however, NTU shall return the payment which has not been consumed in the Research Project to COMPANY without accrued interests. The COMPANY will pay any related additional non-cancellable costs NTU incurred as of the date of termination by the Company.

17Effective Date

17.1 This Agreement shall not become effective until it is executed by the Parties and will be effective on the first date of the Research project as specified in article 2.

17.2 NTU's obligations contemplated in this Agreement shall survive the expiration or termination of this Agreement except for the following clauses: article 10, article 12, article 13, article 14, article 15 and article 17.

18Jurisdiction

In the event that any dispute should arise out of or in connection with this Agreement, the Parties mutually agree to choose Taiwan Taipei District Court as the court of competent jurisdiction at first instance.

19Entire Agreement

19.1 This Agreement with its appendix constitutes the entire and final agreement between the Parties with respect to the subject matter addressed herein. Accordingly, all prior and contemporaneous agreements, understandings, conditions, warranties and representations of any kind, oral or written, are hereby superseded and canceled by this Agreement.

19.2 The appendix shall have the same force and effect as the main Agreement. In the event there is any conflict between the appendix and the main Agreement, the main Agreement shall prevail.

19.3 This Agreement shall be modified or amended with mutual agreement.

19.4 In the event one or part of the clauses in this Agreement is deemed to be invalid by the Court, all other rights, obligations, and provisions of this Agreement shall remain in full validity.

20Copies of the Agreement

This Agreement contains one format of three original copies and three duplicates. The Parties and the Principal Investigator shall each hold one copy. NTU shall hold two duplicates and COMPANY shall hold one duplicate.

IN WITNESS WHEREOF, both NTU and COMPANY have executed this Agreement, in duplicate originals, by their respective and duly authorized officers on the day and year written.

[Signature Page to Follow]

NTU: COMPANY:
NATIONAL TAIWAN UNIVERSITY *Agilis Biotherapeutics, LLC*

By:/s/ Pan-Chyr Yang BY: /s/ Mark J. Pykett
(Signature) (Signature)

NAME: Pan-Chyr Yang NAME: Mark J. Pykett
(in Print) (in Print)
TITLE: President TITLE: President and CEO
DATE: Sep. 30, 2015 DATE: Sep. 30, 2015

Principal Investigator:

BY: /s/ Wuh-Liang (Paul) Hwu
(Signature)

NAME: Wuh-Liang (Paul) Hwu
(in Print)

TITLE: Professor

DATE:

Annex 1
Project

Title: AADC Deficiency Gene Therapy

Abstract: See Annex 2

Period of Performance: October 1, 2015, to September 30, 2017.

Funding: In accordance with Paragraph 3.1 of this Agreement, COMPANY will provide US$[**] in funding to NTU for the Research Costs for the AADC Deficiency Gene Therapy project. Also in accordance with Paragraph 3.12, [**] percent ([**]%) (US$[**]) of Research Cost is for executing the research outlined in Annex 1 and summarized in Paragraph iv below, and [**] percent ([**]%) (US$[**]) of Research Cost is for NTU's overheads. All payments will be made in accordance with Table I below.

Fees Funding of US$[**] shall be payable in connection with the milestones specified in Table I below.

i. US$[**] shall be payable within [**] after the Effective Date of this Agreement being duly signed by the parties.

ii. US$[**] shall be payable [**] within [**] upon reaching milestones [**].

iii. US$ [**] shall be payable within [**] after [**].

iv. The budget for Research Costs shall cover the following:

Clinical study:
[**] subjects at US$[**] (approximately NT$[**]) per the protocol included in Annex 2.
Clinical study monitoring by a qualified Contract Research Organization (CRO) at up to US$[**] (approximately NT$[**]).
Study coordinator: An NTU employee for clinical trial management at US$[**] per year, or US$[**] for [**].
NTU overhead at US$[**].

v. Additionally, Agilis shall also pay for activities pursued by NTU and Dr. Hwu with the University of Florida or other contractors outside of this Agreement in support of the AADC gene therapy program entailing the following work:

[**]

NTU and Agilis shall collaborate to solicit proposals from qualified independent contractors for the rodent biodistribution study and to mutually agree to and select the contractor for this work. NTU and Agilis shall jointly negotiate with the independent contractor to finalize the project plan and budget. NTU shall be the party to engage the selected contractor. Agilis shall pay the agreed-to contract costs directly to the contractor per the contractor's budget and proposal. NTU shall retain all data and reports for this work, and Agilis shall have access to all data and reports.

Research Working Model

- This is a collaborative research project with Professor Wuh-Liang (Paul) Hwu at the National Taiwan University.
- The lead COMPANY scientist is Mark Pykett. Project meeting and updates will be scheduled.

Principal Investigator:
NTU - Dr. Wuh-Liang (Paul) Hwu
National Taiwan University
Taipei, Taiwan
Telephone: +886-____ ext __
Email: ____

COMPANY Technical Contact:
COMPANY - Dr. Mark Pykett
Title: President and CEO
Tel: [**]
Email: [**]

Statement of Work:
Principal Investigator shall oversee the following specific aims and Milestones:

[**].

Table I: Milestone Chart and Schedule

Milestone	Payment
[**]	[**]
[**]	[**]
[**]	[**]
[**]	[**]
[**]	[**]

Annex 2

Phase II clinical study protocol

(The draft version will be subjected to revision according regulatory authorities' review; This contract will be conducted according to the approved version).

Protocol Synopsis

I. Protocol title: A clinical trial for treatment of aromatic-L-amino acid decarboxylase (AADC) deficiency using AAV2-hAADC - An expansion
II. Objectives: This study is to prove the safety and efficacy of AAV2-hAADC treatment for patients with Aromatic L-amino acid decarboxylase (AADC) deficiency.
III. Test drug: **1.** Name: AAV2-hAADC (Lot # [**]) **[**]**
Confidential materials omitted and filed separately with the Securities and Exchange Commission. A total of 3 pages were omitted. [**]

Annex 3

Stability Studies

Scope of Work and Quote for Service by [**]

Date: October 31, 2014
Prepared by: [**]

This Service Agreement is for the Quality Control Testing of rAAV2-CMV-hAADC [**] by the Powell Gene Therapy Center (PGTC), University of Florida. Testing will occur [**]. Testing will be performed according to a [**]. Testing will be [**]. Testing will [**].

Fixed Fee: $ [**]

Note: [**]

Total Cost: $ [**]

Sponsor agrees to pay UF said fixed fee in accordance with the following schedule: invoice will be sent at least [**] prior to testing initiation. To be paid within [**] of invoice.

Costs Not Included: Any activities outside the scope of this contract will be negotiated as a separate charge and invoiced accordingly.

Payment shall be made to the University of Florida and remitted to the following address:

Office of Contracts and Grants
123 Grinter Hall
PO Box: 113001
Gainesville, FL 32611-3001

Investigators: The following are designated as Investigators for the purposes of this Agreement. The Investigators will be responsible for the technical matters of the work plan as outlined in Exhibit A.

For UF: [**]

University of Florida
Pediatrics / CHRI
1200 Newell Drive
ARB RG 187
Gainesville, FL 32610
Telephone: [**]

Annex 4

Representative [**] study and budget required for [**]

NTU and Agilis shall collaborate to solicit proposals from qualified independent contractors for the [**] study and to mutually agree to and select the contractor for this work. NTU and Agilis shall jointly negotiate with the independent contractor to finalize the project plan and budget. NTU shall be the party to engage the selected contractor. Agilis shall pay the agreed-to contract costs directly to the contractor per the contractor's budget and proposal. NTU shall retain all data and reports for this work, and Agilis shall have access to all data and reports.

Proposed Budget for AADC-002 Hwu UNIVERSITY OF FLORIDA GENE THERAPY CENTER NGVL TOXICOLOGY CENTER

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 3 pages were omitted. [**]

Annex 5

[**] Testing

Note: Price valid until [**]					
Assay	**Assay Code**	**Cost/sample**	# **samples**	**Shipping**	**Total Cost**
[**]	[**]	[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]		
[**]	[**]	[**]	[**]		
[**]	[**]	[**]	[**]		
[**]	[**]				
[**]	[**]				
[**]	[**]				
TOTAL DIRECT COST	**[**]**				
INDIRECT [**]%	[**]				
total fixed cost	**[**]**				

Amendment 1

Title: Collaborative Research Agreement
Effective Date: Amendment approval

Original Protocol Statement

3) Research Cost and Payment

3.1 It is agreed to and understood by the parties that NTU shall be paid for the Project and the amount shall be US$[**] (hereinafter "Research Cost"). [**] percent ([**]%) of Research Cost (US$[**]) is for executing the research outlined in Annex 1, and [**] percent ([**]%) of Research Cost (US$[**]) is for NTU's overheads. Additionally, Agilis shall support [**].

3.2 The Research Cost shall be paid by following installment:

3.2.1 US$ [**] shall be payable within [**] after the Effective Date of this Agreement.

3.2.2 US$[**] shall be payable [**] within [**] upon reaching milestones [**].

3.2.3 US$ [**] shall be payable within [**] after [**].

Amended Protocol Statement

3) Research Cost and Payment

3.1 It is agreed to and understood by the parties that NTU shall be paid for the Project and the amount shall be US$[**] (hereinafter "Research Cost"). [**] percent ([**]%) of Research Cost (US$[**]) is for executing the research outlined in Annex 1, and [**] percent ([**]%) of Research Cost (US$[**]) is for NTU's overheads. Additionally, Agilis shall support [**].

3.2 The Research Cost shall be paid by following installment:

3.2.1 US$ [**] shall be payable within [**] after the Effective Date of this Agreement.

3.2.2 US$[**] shall be payable [**] within [**] upon reaching milestones [**].

3.2.3 US$ [**] shall be payable within [**] after [**].

Reason for Change

Agilis will contract directly with an appropriate third party contract research organization to facilitate clinical trial monitoring of the Phase IIb study.

Original Protocol Statement

Annex 1
Project

Title: AADC Deficiency Gene Therapy

Abstract: See Annex 2

Period of Performance: October 1, 2015, to September 30, 2017.

Funding: In accordance with Paragraph 3.1 of this Agreement, COMPANY will provide US$[**] in funding to NTU for the Research Costs for the AADC Deficiency Gene Therapy project. Also in accordance with Paragraph 3.12, [**] percent ([**]%) (US$[**]) of Research Cost is for executing the research outlined in Annex 1 and summarized in Paragraph iv below, and [**] percent ([**]%) (US$[**]) of Research Cost is for NTU's overheads. All payments will be made in accordance with Table I below.

Fees Funding of US$[**] be payable in connection with the milestones specified in Table I below.

i. US$[**] shall be payable within [**] after the Effective Date of this Agreement being duly signed by the parties.

ii. US$[**] shall be payable [**] within [**] upon reaching milestones [**].

iii. US$ [**] shall be payable within [**] after [**].

iv. The budget for Research Costs shall cover the following:

Clinical study:

[**] subjects at US$[**] (approximately NT$[**]) per the protocol included in Annex 2.
Clinical study monitoring by a qualified Contract Research Organization (CRO) at up to US$[**] (approximately NT$[**]).
Study coordinator: An NTU employee for clinical trial management at US$[**] per year, or US$[**] for [**].
NTU overhead at US$[**].

v. Additionally, Agilis shall also pay for activities pursued by NTU and Dr. Hwu with the University of Florida or other contractors outside of this Agreement in support of the AADC gene therapy program entailing the following work:

- [**].

NTU and Agilis shall collaborate to solicit proposals from qualified independent contractors for the rodent biodistribution study and to mutually agree to and select the contractor for this work. NTU and Agilis shall jointly negotiate with the independent contractor to finalize the project plan and budget. NTU shall be the party to engage the selected contractor. Agilis shall pay the agreed-to contract costs directly to the contractor per the contractor's budget and proposal. NTU shall retain all data and reports for this work, and Agilis shall have access to all data and reports.

Research Working Model

- This is a collaborative research project with Professor Wuh-Liang (Paul) Hwu at the National Taiwan University.

- The lead COMPANY scientist is Mark Pykett. Project meeting and updates will be scheduled.

Principal Investigator:
NTU – Dr. Wuh-Liang (Paul) Hwu
National Taiwan University
Taipei, Taiwan
Telephone: +886-_____ ext ___
Email: _____

COMPANY Technical
Contact: COMPANY – Dr. Mark Pykett
Title: President and CEO
Tel: +1-617-444-8706
Email: mpykett@agilisbio.com

Statement of Work:
Principal Investigator shall oversee the following specific aims and Milestones:

[**]

Table I: Milestone Chart and Schedule

Milestone	Payment
[**]	[**]
[**]	[**]
[**]	[**]
[**]	[**]
[**]	[**]

Amended Protocol Statement

Annex 1
Project

Title: AADC Deficiency Gene Therapy

Abstract: See Annex 2

Period of Performance: October 1, 2015, to September 30, 2017.

Funding: In accordance with Paragraph 3.1 of this Agreement, COMPANY will provide US$[**] in funding to NTU for the Research Costs for the AADC Deficiency Gene Therapy project. Also in accordance with Paragraph 3.12, [**] percent ([**]%) (US$[**]) of Research Cost is for executing the research outlined in Annex 1 and summarized in Paragraph iv below, and [**]

percent ([**]%) (US$[**]) of Research Cost is for NTU's overheads. All payments will be made in accordance with Table I below.

Fees Funding of US$[**] be payable in connection with the milestones specified in Table I below.

i. US$[**] shall be payable within [**] after the Effective Date of this Agreement being duly signed by the parties.

ii. US$[**] shall be payable [**] within [**] upon reaching milestones [**].

iii. US$ [**] shall be payable within [**] after [**].

iv. The budget for Research Costs shall cover the following:

Clinical study:
[**] subjects at US$[**] (approximately NT$[**]) per the protocol included in Annex 2.[**]Study coordinator: An NTU employee for clinical trial management at US$[**] per year, or US$[**] for [**].
NTU overhead at US$[**].

Agilis shall separately contract with and pay for clinical study monitoring by a qualified Contract Research Organization (CRO) for the Phase IIb study supported by the sponsored research and outlined in Annexes 1 and 2 at its own costs of to US$[**] (approximately NT$[**]).

v. Additionally, Agilis shall also pay for activities pursued by NTU and Dr. Hwu with the University of Florida or other contractors outside of this Agreement in support of the AADC gene therapy program entailing the following work:
[**]

NTU and Agilis shall collaborate to solicit proposals from qualified independent contractors for the rodent biodistribution study and to mutually agree to and select the contractor for this work. NTU and Agilis shall jointly negotiate with the independent contractor to finalize the project plan and budget. NTU shall be the party to engage the selected contractor. Agilis shall pay the agreed-to contract costs directly to the contractor per the contractor's budget and proposal. NTU shall retain all data and reports for this work, and Agilis shall have access to all data and reports.

Research Working Model

- This is a collaborative research project with Professor Wuh-Liang (Paul) Hwu at the National Taiwan University.
- The lead COMPANY scientist is Mark Pykett. Project meeting and updates will be scheduled.

Principal Investigator:
NTU – Dr. Wuh-Liang (Paul) Hwu
National Taiwan University
Taipei, Taiwan
Telephone: +886-_____ ext ___
Email: _____

COMPANY Technical Contact:
COMPANY – Dr. Mark Pykett
Title: President and CEO
Tel: [**]
Email: mpykett@agilisbio.com

Statement of Work:
Principal Investigator shall oversee the following specific aims and Milestones:

[**].

Table I: Milestone Chart and Schedule

Milestone	Payment
[**]	[**]
[**]	[**]
[**]	[**]
[**]	[**]
[**]	[**]

Reason for Change
Agilis will contract directly with an appropriate third party contract research organization to facilitate clinical trial monitoring of the Phase IIb study.

(signature) Date
National Taiwan University
Representative:
Address: No. 1, Section 4, Roosevelt Road, 106 Taipei City

Paul Wuh-Liang Hwu, M.D., Ph.D. Date
Sponsor
National Taiwan University Hospital

/s/ Mark J. Pykett July 6, 2016
Mark J. Pykett, V.M.D., Ph.D. Date
CEO
Agilis Biotherapeutics

Collaborative Research Agreement
Amendment 2

This Amendment 2 is made and entered into as of the last date signed below (the "Amendment 2 Effective Date") to that certain Collaborative Research Agreement dated September 30, 2015 (as amended, the "Agreement") by and between National Taiwan University at No. 1, Sec. 4, Roosevelt Road, Taipei, 10617 Taiwan (R.O.C) (hereinafter "NTU") and Agilis Biotherapeutics, LLC, a Delaware limited liability company duly organized under law and having an address at 245 First St, Suite 1800, Cambridge, MA, 02142 USA (hereinafter "COMPANY"). Capitalized terms herein shall have the meaning ascribed to them in the Agreement.

Per the terms of Section 5 of the Agreement, the COMPANY and NTU hereby agree to a one year extension of the Term from September 30, 2017 to September 30, 2018.

AGILIS BIOTHERAPEUTICS, LLC	NATIONAL TAIWAN UNIVERSITY
By: /s/ Mark J. Pykett Authorized Signature	By: _ Authorized Signature
Mark J. Pykett, VMD, PhD, CEO	_ Printed Name & Title
December 20, 2016 Date	_ Date

Collaborative Research Agreement
Amendment 3

This Amendment 3 is made and entered into as of the last date signed below (the "Amendment 3 Effective Date") to that certain Collaborative Research Agreement dated September 30, 2015 (as amended , the "Agreement") by and between National Taiwan University at No. 1 , Sec. 4, Roosevelt Road, Taipei, 10617 Taiwan (R.O.C) (hereinafter "NTU") and Agilis Biotherapeutics, Inc., a Delaware corporation duly organized under law and having an address at 245 First St, Suite 1800, Cambridge , MA, 02142 USA (hereinafter "COMPANY"). Capitalized terms herein shall have the meaning ascribed to them in the Agreement.

Per the terms of the Agreement, the COMPANY and NTU hereby agree to add a [**] subject to the AADC Phase II clinical study to be enrolled under and treated by the existing Phase II clinical protocol, and requiring all appropriate patient consents, including the signing of an informed consent form, for an added cost of US$[**] (approximately [**] NTD).

AGILIS BIOTHERAPEUTICS	NATIONAL TAIWAN UNIVERSITY
By: /s/ Mark J. Pykett _ Authorized Signature	By: /s/ Ching Ray Chang Authorized Signature

Mark J. Pykett, VMD, PhD, CEO

Printed Name & Title

June 12, 2017
Date

Date:

Collaborative Research Agreement
Amendment 4

This Amendment 4 is made and entered into as of the last date signed below (the "Amendment 4 Effective Date") to that certain Collaborative Research Agreement dated September 30, 2015 (as amended, the "Agreement") by and between National Taiwan University at No. 1, Sec. 4, Roosevelt Road, Taipei, 10617 Taiwan (R.O.C) (hereinafter "NTU") and Agilis Biotherapeutics, a Delaware corporation duly organized under law and having an address at 245 First St, Suite 1800, Cambridge, MA, 02142 USA (hereinafter "COMPANY"). Capitalized terms herein shall have the meaning ascribed to them in the Agreement.

Per the terms of Section 5 of the Agreement, the COMPANY and NTU hereby agree to a three year extension of the Term from October 1, 2017 to September 30, 2020. This Amendment 4 supersedes Amendment #2 (which was a one-year, no cost extension from September 30, 2017 to September 30, 2018).

Research Technical Objectives of Amendment 4:

[**]

Budget:

- Per Section 3.1 of the Agreement, it is agreed to and understood by the parties that NTU shall be paid for the Project and the amount of Amendment #4 for the Research Cost shall be approximately NTD [**] for executing the Research and Technical Objectives outlined above in this Amendment #4. [**] percent ([**]%) of Research cost in the amount is for the Technical Objectives, and [**] percent ([**]%) of Research Cost is for NTU' s overheads.

- Per Section 3.2 of the Agreement, the Research Cost shall be paid by following installment Payments on the agreed budget shall be made to NTU in [**] installments in NTD as follows, subject to the Technical Objectives being met
    - Year one: approximately [**] at within [**] of signing Amendment #4 and [**].
    - Year two: approximately [**] at [**].
    - Year three: approximately [**] at [**] and within [**] of the September 30, 2020 contract end.

AGILIS BIOTHERAPEUTICS

By: /s/ Mark J. Pykett
Authorized Signature

Mark J. Pykett, VMD, PhD, CEO

September--, 2017
Date

NATIONAL TAIWAN UNIVERSITY

By: /s/ Teiwei Kwo
Authorized Signature

Printed Name & Title

Date

Study				**case number**	**test per year**	**unit price (NTD)**	**Cost per year (NTD)**	**Total Cost 3 years (NTD)**	
[**]	[**]			[**]	[**]	[**]	[**]	[**]	
[**]	[**]	[**]	[**]	[**]	[**]	[**]	[**]	[**]	
		[**]	[**]	[**]	[**]				
		[**]			[**]				

	[**]	[**] [**]			[**] [**]	[**] [**]	[**]	[**]	
[**]	[**]					[**]	[**]	[**]	
[**]	[**]						[**]	[**]	
[**]	[**]						[**]	[**]	
	[**] [**] [**]						[**] [**]	[**] [**]	[**]
	[**]				[**]		[**]	[**]	[**]
							[**]	[**]	[**]

Exhibit 10.4

License and Technology Transfer Agreement

LICENSED TECHNOLOGY: AADC Gene Therapy

Licensor: National Taiwan University
Inventor: Professor Wuh-Liang (Paul) Hwu
Licensee: Agilis Biotherapeutics, LLC
NTU Contract No.: _____

All results from conducted research and development belong solely to National Taiwan University.

Type of Contract	License and Technology Transfer Agreement (Research and development results belong solely to NTU)	Contract No.	□□□□□□□□□
Licensed Technology	□□□□□□□□□□□□□□□□□		

09TTA01

License and Technology Transfer Agreement

(the "Agreement")

Effective Date: December 23, 2015

Parties to Agreement:

National Taiwan University (hereinafter "Party A")

Professor Wuh-Liang (Paul) Hwu (hereinafter "Party B")

Agilis Biotherapeutics, LLC (hereinafter "Party C")

WHEREAS, Party B has already developed, invented, and/or made practical technology through utilizing resources and research facilities provided by Party A.

WHEREAS, Party A owns all intellectual property directly or indirectly related to the Technology as defined in Article 2.

WHEREAS, Party A desires to grant Party C a license to use or implement the Technology in the territories as defined below as currently existing Technology as well as to be further developed as described herein.

WHEREAS, the Parties entered into a certain Collaborative Research Agreement dated as of September 30, 2015 (the "Research Agreement"), and Party C is funding the research and development of the Technology that is being exclusively licensed to Party C in accordance with the terms and conditions of this Agreement.

NOW, THEREFORE, in consideration of the mutual covenants and agreements herein contained and for other good and valuable consideration, including the herein promises, agreements, representations and warranties, the receipt of legal sufficiency of which is hereby acknowledged, accepted and agreed to, the Parties, intending to be legally bound, hereby agree as follows:

Article 1: Technology; Title and Ownership

1.1 This Technology is in existence and also being developed and invented by Party B and Party C in the course of the execution of a Collaborative Research Agreement dated as of September 30, 2015 (hereinafter the "Research Agreements"). All of the intellectual property, data and research results are collectively referred to as the "Research Results"). Subsidized Research Project "Collaborative Research Agreement" (project number: [**]). Party A owns all rights, title, and interest in the Technology as well as all intellectual property rights vested therein.

Article 2: Construction and Definitions

2.1 "Technology" means any and all intellectual property (including all patents patent applications any continuations, divisional, and continuations in-part, any reissues, re-examinations, extensions or substitutions of the patents, and the relevant international equivalents), data, CMC records, documents, confidential information, materials and know-how pertaining to the AADC gene therapy product and existing on the date of this Agreement and otherwise relating to the Research Results as detailed in Attachment I and Research Agreement. The Parties acknowledge and agree that a portion of the Technology exists as of the Effective Date and a portion of the Technology will be developed and created as the work under the Research Agreement is completed. Accordingly, the Parties agree that Attachment I will automatically be amended and supplemented, from time to time as the Research Agreement is completed and all additional Technology will be automatically added to Attachment I. For convenience, Section A of Attachment I contains a listing of the existing Technology and Section B of Attachment I lists all of Technology developed to date pursuant to the Research Agreement. Section B of Attachment I will be updated from time to time.

2.2 Intentionally Omitted.

2.3 "Licensed Area" means all countries of the world.

2.4 "Effective Date" means December 23, 2015.

2.5 "Due Date" means [**] after the Effective Date.

2.6 Scope of Licensed Implementation: The exclusive license covers the Technology, which is all intellectual property, data, CMC records, documents, materials, trade secrets, confidential information and know-how pertaining to the AADC gene therapy product existing as of the Effective Date and otherwise relating to the Research Results and Research Agreement. Party C is hereby granted an exclusive, perpetual license with the right to grant sub-licenses through all tiers, to research and use the Technology and to develop, have developed, make, have made, manufacture, have manufactured, use, sell, have sold, offer for sale, import for the above purposes and market Licensed Products which are made, invented, developed, or incorporated by or with the Technology in the Licensed Area.

2.7 Licensed Product: AADC gene therapy and related products which are made, invented, developed, incorporated by or with developed from utilizing the Technology.

2.8 “License Period” means the duration of the exclusive license granted by this Agreement.

2.9 License Method: This Agreement grants an exclusive, perpetual license, provided that Party A may still implement the Licensed Technology for internal, non-commercial purposes only and solely limited to academic research.

2.10 “Net Sales” means the gross revenues received by Party C, and sublicensees from the sale of any Licensed Product less: (i) sales and/or use taxes actually paid, import and/or export duties and other governmental charges actually paid, (ii) outbound transportation paid, prepaid or allowed, (iii) amounts allowed or credited, and actually refunded, due to returns (as reflected on the invoice, and not to exceed the original billing amount), (iv) rebates, trade, quantity and cash discounts to purchasers allowed and taken (v) insurance, handling or shipping charges to purchasers.

Article 3: Transfer and Implementation of Technology

3.1 Transfer of Technical Information: Party B shall provide all necessary information, know-how, trade secrets and confidential information regarding the Technology to Party C within [**] from the Effective Date of this Agreement.

3.2 Product Commercialization Deadline: Subject to any regulatory delays or issues, Party C shall research, use and develop the Technology to manufacture have manufactured, import, have imported and sell, or have sold, manufactured products within [**] from the Effective Date of this Agreement pursuant to the Development Plan proposed by Party C (detailed in Attachment II, which may be amended from time to time as the Research Agreement progresses). Party C shall guarantee that it has sufficient financial means and operational facilities to commercialize the Technology and shall use commercially reasonable efforts for the marketing of the Licensed Products. If there is any delay or cessation of the Development Plan, Party C shall immediately notify Party A and Party B in writing and within [**], Party C shall present a revised Development Plan to Party A and Party B accounting for the development factors impacting on the commercialization of the Licensed Products.

3.3 Initiation of the first Phase III study (defined as enrollment of the first patient as noted by the signing of the informed consent form by the patient) shall commence no later than [**]. Completion of the first Phase III study using the Technology shall occur no later than [**]. Successful registration of the Technology in the United States by the FDA or in Europe by the EMA shall occur no later than December 31, 2024.

Article 4: Obligations and Liabilities

4.1 Instructive Consulting: Party B shall provide Party C with a total of [**] of technical instruction and consultation within [**] immediately following the transfer of technical information to Party C as noted in Article 3.1 hereof. Exceeding these hours or upon Party C’s request for further detailed consultation services or personnel training regarding the Technology shall incur a technical service fee payable to Party B. The time, location, fee, and method of consultation shall be further negotiated by Party B and Party C.

4.2 **CONFIDENTIALITY CLAUSE**: Any information related to the Technology and/or the terms of this Agreement itself will be considered Confidential Information.

Except as required to commercialize the Licensed Products or otherwise satisfy its obligations hereunder; Party C agrees to exercise due care in keeping confidential any and all information related to the Technology, including any and all documentation and other physical manifestations or embodiments thereof. The confidentiality obligations under this Agreement shall survive for a period of [**] after termination or expiration of this Agreement.

Article 5: Calculation and Payment Terms for License Fee and Royalty

5.1 Royalty: During the Term hereof, Party C shall pay to Party A, a royalty based on Net Sales of the Licensed Products including the Technology in the Licensed Area. The Royalty on Net Sales shall be [**] percent ([**]%) on the sale of Licensed Products. Following the Term (as defined in Article 9), Party C shall be automatically granted an exclusive, royalty-free perpetual license to practice the Technology and sell License Products anywhere in the Licensed Area without the payment of a Royalty or other fee or consideration.

5.2 Up-front payments, milestone payments and funding for Phase III (or pivotal trial).

5.2.1 Upon signing this Agreement, Party C shall pay Party A an up-front fee of US$100,000.00. Unless this Agreement is early terminated by Party C in accordance with Section 9.1 hereof, Party C shall commit to funding a Phase III clinical study in AADC deficiency using the Technology for an estimated [**] subjects as approved by Party C. The study will be conducted at least in part in Taiwan; however, for purposes of enabling registration in other countries, the Phase III clinical study may also be conducted in other countries as well.

5.2.2 Upon Initiation of the first Phase III study (defined as enrollment of the first patient as noted by the signing of the informed consent form by the patient) using the Technology, Party C shall pay Party A a milestone fee of US$[**].

5.2.3 Upon completion of the first Phase III study using the Technology, Party C shall pay Party A a milestone fee of US$[**].

5.2.4 Upon successful registration of the Technology in the United States by the FDA or in Europe by the EMA, Party C shall pay Party A a milestone fee of US$[**].

5.3 License Maintenance Fee. Beginning on the first (1st) anniversary of the Effective Date of this Agreement and for each anniversary thereafter, Party C will pay Party A the following yearly maintenance fees:

5.3.1 US $[**] on the [**] anniversaries;

5.3.2 US $[**] on the [**] anniversaries;

5.3.3 US $[**] on the [**] anniversaries; and

5.3.4 US $[**] for the [**] and each anniversary thereafter until the 20th anniversary.

5.3.5 Yearly maintenance fees are nonrefundable, but are fully creditable against Royalties payable pursuant to Section 5.1 hereof.

5.4 Royalty and Maintenance Fee Term. The Maintenance Fees noted in Section 5.3 and the Royalty noted in Section 5.1 shall be in effect for a period of twenty (20) years from the Effective Date of this Agreement.

5.5 Sublicenses: Party C shall pay Party A [**]%) percent of any up-front fee received from a sublicensee and [**]%) percent of any milestone fee received from a sublicensee, but that all fees paid to Party C for: (i) R&D, (ii) for the sale by Party C of its own common or preferred stock on usual and customary terms with a purchase price that represents the fair market value of the shares being purchased or (iii) reimbursement of patent expenses and fees shall not be subject to the sub-licensing fees. If Party C sublicenses this Agreement, the sublicensee must be responsible for all the terms in execution of this Agreement on behalf of Party C including but not limited to clinical trials, regulatory registration, upfront payment, milestone payment, royalty and license maintenance fees.

5.6 Patents: Party C will, with advice and input from Party A, prepare, file, prosecute and maintain all of the patent applications and patents including the Technology with counsel selected by Party C and reasonably acceptable to Party A. Party A agrees that it will not abandon any of the patent applications or patents in any county without the prior written consent of Party C. Party C will be responsible for the reasonable costs of preparing, filing, presenting and maintaining said patent applications and patents. If Party A or Party C decides to discontinue its support for any patent applications or patent covered by this Agreement, it shall provide the other Party with written notice of such intention to discontinue its support for any patent application or patent and the Parties shall mutually decide, in or within [**] of that notice, of their decision as to whether or not they wish to continue supporting the patent applications or patents or allow the patent or patent applications to be abandoned. If the Parties are unable to reach an agreement, for whatever reason, then the Party wishing to continue the support shall solely be responsible for all subsequent costs and expenses associated therewith after the other party discontinue support for the patent.

5.7 Payment Terms: Party C shall make payments to Party A pursuant to Sections 5.1 and 5.2 of this Article in cash or check. If any payment needs to be withheld for tax purposes, it shall be handled in accordance with the current tax code.

5.8 If deemed necessary, but not more often than [**] and subject to entering into a usual and customary Confidential Agreement, Party A is entitled to dispatch accounting personnel or qualified accountants to Party C’s main business location during normal business hours for purposes of auditing sales income from Licensed Products. Party C hereto agrees to take or cause to be taken all such other cooperative actions as are reasonably necessary or desirable in order to permit the other parties to obtain the full benefits of this Agreement. Party C shall also retain relevant bookkeeping records for [**] following the termination of this Agreement for Party A’s use to confirm the accuracy of the Royalty payments. Party A’s acceptance of the royalty as compiled and reported by Party C does not affect Party A’s right to make a subsequent verification of Party C’s report. If discovered that Party C reported a lower amount in royalties than the actual fee reported in audits from Party A’s bookkeeping records, Party C shall make recompensation for the difference and any interest thereof at rate of [**]%) percent

per annum. If the difference exceeds [**]%) percent of the amount payable by Party C, Party C shall also be liable for Party A's reasonable audit fees.

5.9 The amounts of the above-mentioned license fee and royalty as listed above are inclusive of business tax.

Article 6: Attribution of Intellectual Property Right and Infringement Liability

6.1 All intellectual property rights that relate to the manufacture, production, assembly, use or sale of the Technology and any Licensed Products derived thereof are vested solely in Party A. Subject to the terms and conditions of this Agreement, Party C is granted an exclusive license as more fully noted in Section 2.6 hereof. Party A is not entitled to enter into another technology license and transfer agreement with any third parties covering or related to the Technology or Research Results.

6.2 In the event that Party A or Party B believes that Party C has violated this Agreement, the parties shall meet and, in good faith, use their best efforts to resolve any dispute or disagreement. If after [**], the parties are unable to resolve the dispute or disagreement, the matter shall be referred to final and binding arbitration in accordance with Section 14.3 hereof.

6.3 If Party C wishes to incorporate a derivative for the development of the Technology, Party C shall provide [**] prior notice in writing to Party A and Party B. Only upon Party A and Party B's consent, which consent shall not be unreasonably withheld or delayed, may Party C transfer information regarding the Technology to the derivative by sub-license or enter into another contractual agreement.

6.4 In the case of any patent infringement action or any third party claim or suit in Party C's sale of Licensed Products manufactured by use of the Technology, Party C shall notify Party A and Party B as soon as possible and shall make its best efforts to carry out necessary defensive strategies to protect the common interests of the three (3) parties.

6.5 In the case of any patent infringement under this Agreement and if any claim should be made or litigation to be filed, Party C shall immediately notify Party A and Party B and shall make its best efforts to assist Party A and Party B in taking protective

measures and Party A (and Party B if applicable), shall, in a timely manner, institute legal proceedings in order to protect the common interests of the three (3) parties.

6.6 All of the intellectual property rights of derivative or additional research, developed or added by Party C shall belong to Party C. Based on the principle of mutual benefit, Party A shall be notified and granted a non-exclusive, non-assignable right related to the intellectual property rights for Party A to use internally, for academic purposes only provided that Party A and Party B shall not disclose, deliver, or make available any such technical information to any third party. Party A and Party B shall not be held liable in any infringement proceeding involving intellectual property rights developed from derivative research. Party C shall defend, indemnify, and hold Party A harmless against all claims, suits, proceedings, losses, liabilities, and damages (including costs, expenses, and reasonable attorneys' fees) arising from: (i) any unauthorized use or dissemination of the Technology by Party C and (ii) any violation of this Agreement or of any third-party's rights by Party C, including but not limited to infringement of any copyright, violation of any proprietary right and invasion of any privacy right.

6.7 Licensed Products manufactured by Party C based on the Technology shall be properly labeled in accordance with relevant laws of the particular country in which the Licensed Products are going to be sold. Party A and Party B shall not be held liable for any product liability suit involving such products. Party C shall indemnify and hold harmless Party A and Party B against all claims, suits, proceedings, losses, liabilities, and damages (including costs, expenses, and reasonable attorneys’ fees) asserted by third parties against Party A which arise out of any act or omission by Party C.

6.8 Party C shall clearly mark “patent pending” on the Licensed Products manufactured from the Technology and their packaging containers if an application for patent on Research Results has been filed and such patent has not yet been granted. After the patent for the Research Results has been granted, the patent certificate number shall be clearly marked.

Article 7: No Warranty Clause

7.1 The Technology will be provided “AS IS” and delivered to Party C in electronic form or hard copy by Party B from time to time when requested by Party C Party A and Party B guarantee that they will make their best efforts to assist Party C in

use of the Technology and Party A represents and warrants that it has full right, title, interest and ownership to the Technology and Parties A and B represent and warrant that they both have the right and authority to enter into this Agreement. Save as provided above, Party A gives no warranty, express or implied, and makes no representation that: (i) the Technology will be of satisfactory quality, suitable for any particular purpose or for any particular use under specified conditions, notwithstanding that such purpose, use, or conditions may be known to Party A; or (ii) that the Technology will operate error free or without interruption or that any errors will be corrected; or (iii) that the material published in the Technology is either complete or accurate. Furthermore, no warranties are given for the patentability, fitness for particular purpose, or merchantability of the Technology.

7.2 All technical information obtained by Party C shall be treated as confidential and shall be protected in the manner of trade secrets. Any damage or infringement occurring after the implementation of the Technology shall be Party C's responsibility, provided that Party A and Party B shall make their best efforts to assist Party C for handling such matters.

Article 8: Breach of Contract

8.1 Party C's failure to pay any undisputed license fee and Royalty within the deadline provided under Article 5 hereof may constitute a basis for Party A terminating this Agreement subject to Party C's right to arbitration in accordance with Section 14.3 hereof. Party A shall notify Party C of any alleged breach and Party C shall have thirty (30) days to cure the alleged breach and if cured, then Party A shall have no right of termination and if not cured, then Party A may terminate subject to Party C's right to request arbitration.

8.2 In case of any breach of material obligation by Party A and/or Party B, Party C may notify Party A and Party B of such breach and Party A and/or B shall have thirty (30) days after receipt of the notice to cure such breach and if cured, then Party C shall have no right of termination and if not cured, then Party C may terminate subject to Party A and Party B's right to request arbitration.

8.3 In no event shall any party be liable for any indirect, special or consequential damages, including without limitations, lost profits and lost revenue.

Article 9: Term of Agreement

9.1 This Agreement shall become effective on the Effective Date and shall expire twentieth (20th) anniversary of this Agreement; and thereafter, Party C shall have a fully paid up, perpetual, royalty-free exclusive license in accordance with Article 5.1 hereof. Nothwithstanding the foregoing, in the event of a failure of a pivotal clinical study or a serious adverse event in a clinical study that prevents development from continuing under reasonable circumstances, or the rejection of a Biologics License Application with the US FDA, a Marketing Authorization Application with the European EMA, or equivalent biologics approval application in another territory with the relevant regulatory authority, Party C may terminate this Agreement at any time upon sixty (60) days prior written notice to Party A and upon the expiration of the aforesaid sixty (60) day period, this Agreement shall terminate and be null and void except for those provisions which survive in accordance with their terms. Under conditions in which Party C has terminated the Agreement, Party A will retain all rights to the Technology, including the exclusive use of any and all intellectual property (including all patents patent applications any continuations, divisional, and continuations in-part, any reissues, re-examinations, extensions or substitutions of the patents, and the relevant international equivalents), data, CMC records, documents, confidential information, materials and know-how pertaining to the AADC gene therapy product and existing on the date of this Agreement and otherwise relating to the Research Results as detailed in Attachment I and Research Agreement. Additionally, in good faith and recognizing that Party B may desire to continue the program without Party C, if Party C terminates the Agreement, Party C agrees to pay to Party A the sum of US$100,000.00 and to provide copies of all documents and materials in its possession related to the Technology within thirty (30) days of termination.

9.2 Termination or expiration of this Agreement shall not affect any rights or obligations accrued prior to such termination or expiration, or any obligations which are stated herein to survive such termination or expiration.

Article 10: Effect of Expiration

10.1 Party C shall return to Party A the technical information obtained from Party A and Party B and pay the Royalty due in full within [**] of the expiration of this Agreement.

10.2 After the expiration of this Agreement, Party C shall refrain from any production or manufacture by itself or through another person by use of the Technology. However, if Party C has substantial proof to show that the product was manufactured prior to the expiration or termination of this Agreement, the sale of the Licensed Product may continue until all work in progress has been completed and the inventory has been sold, provided that the royalty shall remain payable pursuant to Article 5.

10.3 The obligations of Party C as set out in Articles 4, 5, (only with respect to the continuation of sale pursuant to Section 10.2), and 6 will survive the termination or expiration of this Agreement.

10.4 After the expiration or termination of this Agreement, or any extension thereof, Party C shall return all intellectual property, technology, confidential information and know-how related to the patents and patent applications to Party A.

Article 11: Amendment to Agreement

11.1This Agreement may be amended in writing upon consent of all three parties, provided, that this Agreement may be amended only by Parties A and C to the extent such amendment does not impair Party B's rights hereunder. The amended document signed by all three parties shall be attached to this Agreement as an integral part hereof and shall replace the original provisions which have been amended and replaced.

Article 12: Contract Performance Guarantee

12.1 If Party C is unable to commercialize the manufactured products manufactured by use of the Technology within the fixed deadline as set forth in Article 3.2 hereof, Party C will provide written notice to Party A and Party B and the Parties shall meet and establish a revised Development Plan in accordance with Section 3.2 hereof.

Article 13: Governing Law and Arbitration

13.1 This Agreement shall be construed in accordance with and governed by the laws of the Republic of China□Taiwan).

13.2 The three (3) parties agree that any controversy or dispute arising in connection with this Agreement shall first be resolved under the principle of good faith within [**] after a party serves a notice of dispute on the other parties.

13.3 In the event that any matter cannot be resolved in accordance with Section 14.2 hereof, then the matter shall be referred to arbitration for resolution before a single arbitrator under the then commercial arbitration rules of the International Chamber of Commerce (the "I.C.C.") If the parties are unable to agree on a single neutral arbitrator, such arbitrator shall be appointed by the I.C.C. The arbitrator shall not have any current or past business or financial relationships with any party to the arbitration, and shall have experience in the arbitration or mediation of contract disputes. Each party shall be responsible for its proportionate share of the filing fee and the arbitrator's fee; and otherwise, each party shall be responsible for its own costs and expenses, including travel, consultants, witnesses and attorneys' fees and disbursements. The arbitrator shall be authorized only to interpret and apply the provisions of this Agreement or any related agreements entered into under this Agreement and shall have no power to modify or change any of the above in any manner. The arbitrator shall have no authority to award punitive, special or consequential damages or any damages inconsistent with this Agreement. The arbitrator shall, within [**] of the conclusion of the hearing, unless such time is extended by agreement of the parties, notify the parties in writing of his or her decision, stating his or her reasons for such decision and separately listing his or her findings of fact and conclusions of law. The arbitration shall be conducted in Los Angeles, California, and shall be governed by the laws of the Republic of China (Taiwan), and the decision of the arbitrator shall be final and binding and may be entered in any court of competent jurisdiction. To the extent permitted by applicable laws, nothing in this Section 14.3 shall in any way limit the right of a party to seek preliminary injunction from the Taipei District Court pending an award being issued. The parties agree that all applicable statutes of limitation and time based defenses (i.e. estoppel and laches) shall be tolled whole the procedures set forth in this Section 14.3 are pending. The parties shall cooperate in taking any actions necessary to achieve this result. Each party shall continue to perform its undisputed obligations under this Agreement pending resolution of any dispute arising out of or relating to this Agreement.

Article 14: Contact Management

14.1 Notice or request related to this Agreement shall be in writing and delivered to the following locations and persons (hereinafter the “Contact Person”) and shall be deemed received by the corresponding party when it is delivered to the Contact Person:

Party A Contact Person: Andrew Man-Chung Wo
Title: Director of Center of Industrial-Academic Cooperation
Telephone: [**] Fax: [**]
Address: Center of Industrial-Academic Cooperation, No. 18 Si Yuan Street, 100 Taipei City

Party B Contact Person: Wuh-Liang Hwu (Paul),
Title: M.D., Ph.D
Telephone: [**]
Fax: [**]
Address: Department of Pediatrics and Medical Genetics Room 19005, 19F,
Children’s Hospital Building National Taiwan Unversity Hospital
8 Chung-Shan South Road, Taipei 10041, Taiwan

Party C Contact Person: Dr. Mark J. Pykett
Title: President and CEO
Telephone: [**]
Fax: [**]
Address: 245 First Street, Suite 1800, Cambridge, MA 02142
Email: [**]

In the case of any changes made to any Contact Person or contact information, a written notice shall be sent to the other two (2) parties for update.

Article 15: Copies of Agreement

This Agreement is made in four original copies, with Party A retaining two copies and Party B and Party C each retaining one copy.

---------- Signature Page Follows ----------

Parties to Agreement

Party A: National Taiwan University

Representative: Pan-Chyr Yang

Address: No. 1, Section 4, Roosevelt Road, 106 Taipei City

_/s/ Pan-Chyr Yang_____ _____

(signature) (date)

Party B: Professor Wuh-Liang (Paul) Hwu

Current Department: Pediatrics

Title: Professor

_/s/ Wuh-Liang Hwu_____ 23 Dec 2015_____

(signature) (date)

Party C: Agilis Biotherapeutics, LLC

Federal Tax ID No. (EIN): 46-3936833 (USA)

Address: 245 First St, Suite 1800, Cambridge, MA 0-2142 USA

Representative: Dr. Mark J. Pykett

Title: President and CEO

By: _/s/ Mark Pykett__ 21 December 2015

(signature) (date)

Attachment I Contents of Licensed Technology

Name of Technology: AADC Deficiency Gene Therapy

Type of Intellectual Property: ▪ Know-how

☐ Patent

☐ IC Layout

☐ Plant Root

☐ Copyright

☐ Trademark

▪ Others: data, CMC records, documents, confidential information, and materials

Inventor: Wuh-Liang Hwu

Summary Description of License:

[**]

Attachment II Development Plan of AGILIS BIOTHERAPEUTICS, LLC

AAV-hAADC Gene Therapy
Development Plan

Background

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 3 pages were omitted. [**]

Exhibit 10.5

Confidential Materials omitted and filed separately with the
Securities and Exchange Commission. Double asterisks denote omissions.

COLLABORATION AND LICENSE AGREEMENT

By and between

PTC THERAPEUTICS INTERNATIONAL LIMITED

AND

AKCEA THERAPEUTICS, INC.

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This COLLABORATION AND LICENSE AGREEMENT (the "**Agreement**") is entered into and made effective as of August 1, 2018 (the "**Effective Date**"), by and between **PTC THERAPEUTICS INTERNATIONAL LIMITED**, an Irish corporation, having its principal place of business at 5th Floor, 3 Grand Plaza, Grand Canal Street Upper, Dublin 4, Ireland D04 EE70 ("**PTC**"), and **AKCEA THERAPEUTICS, INC.**, a Delaware corporation, having its principal place of business at 55 Cambridge Parkway, Suite 100, Cambridge, MA 02142 ("**Akcea**"). PTC and Akcea shall be referred to herein individually as a "**Party**" and collectively as the "**Parties**".

RECITALS

WHEREAS, PTC and Akcea are biopharmaceutical companies focused on developing, manufacturing and commercializing drugs for rare diseases on a global basis;

WHEREAS, PTC is a wholly-owned indirect subsidiary of PTC Therapeutics, Inc., a Delaware corporation ("**PTC Parent**");

WHEREAS, Akcea has in-licensed certain worldwide rights from its Affiliate (as defined below) Ionis Pharmaceuticals (as defined below) to develop, manufacture and commercialize inotersen (proposed to be marketed as TEGSEDI™) and volanesorsen (proposed to be marketed as WAYLIVRA™);

WHEREAS, Ionis Pharmaceuticals is currently seeking regulatory approval for inotersen and volanesorsen and intends to assign its Regulatory Filings and Regulatory Approvals (each, as defined below) to Akcea;

WHEREAS, Akcea and PTC desire to engage in a collaborative effort with respect to the development and commercialization of inotersen and volanesorsen by PTC in the PTC Territory (as defined below) and by Akcea in the rest of the world outside of the PTC Territory;

WHEREAS, Akcea also wishes to grant to PTC, and PTC wishes to obtain, certain rights of first negotiation with regard to the commercialization in the PTC Territory of AKCEA-TTR-L_{Rx}, a follow-on product to inotersen.

NOW, THEREFORE, in consideration of the premises and mutual covenants herein contained, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties agree as follows:

ARTICLE 1
DEFINITIONS

As used in this Agreement, the following terms will have the meanings set forth below:

1.1 "**Affiliate**" means any Person that, directly or indirectly through one or more intermediaries, controls, is controlled by or is under common control with a Party to this Agreement, regardless of whether such Affiliate is or becomes an Affiliate on or after the Effective Date. A Person shall be deemed to "control" another Person if it (a) owns, directly or indirectly, beneficially or legally, more than fifty percent (50%) of the outstanding voting securities or capital stock of such other Person, or has other comparable ownership interest with respect to any Person other than a corporation; or (b) has the power, whether pursuant to contract, ownership of securities or otherwise, to direct the management and policies of such other Person. For the avoidance of doubt, Ionis Pharmaceuticals and Akcea shall constitute an "Affiliate" of each other for purposes of this Agreement and PTC and PTC Parent shall constitute an "Affiliate" of each other for purposes of this Agreement.

1.2 "**Akcea Core Technology IP**" means the Akcea Core Technology Know-How and the Akcea Core Technology Patent Rights.

1.3 "**Akcea Core Technology Know-How**" means all Know-How Controlled by Akcea or its Affiliates on the Effective Date or at any time during the Term that (a) is necessary to Develop or Commercialize a Product and (b) relates generally to oligonucleotides including Conjugate Technology, other than Know-How specifically relating to a Product (including Akcea Product-Specific Know-How) or Know-How specifically relating to methods and materials used in the synthesis or analysis of a Product regardless of sequence or chemical modification.

1.4 "**Akcea Core Technology Patent Rights**" means all Patent Rights Controlled by Akcea or its Affiliates on the Effective Date or at any time during the Term that (a) is necessary to Develop or Commercialize a Product, and (b) claims subject matter generally applicable to oligonucleotides including Conjugate Technology, other than Akcea Product-Specific Patent Rights or Patent Rights that claim methods and materials used in the synthesis or analysis of a Product regardless of sequence or chemical modification. The Akcea Core Technology Patent Rights as of the Effective Date are set forth on Schedule 1.4 attached hereto.

1.5 "**Akcea IP**" means the Akcea Core Technology IP, the Akcea Manufacturing IP and the Akcea Product-Specific IP.

1.6 "**Akcea Manufacturing IP**" means the Akcea Manufacturing and Analytical Know-How and the Akcea Manufacturing Patent Rights.

1.7 "**Akcea Manufacturing and Analytical Know-How**" means Know-How that relates to the synthesis or analysis of a Product regardless of sequence or chemical modification Controlled by Akcea or its Affiliates on the Effective Date or at any time during the Term.

1.8 "**Akcea Manufacturing Patent Rights**" means the Patent Rights that claim Akcea Manufacturing and Analytical Know-How. The Akcea Manufacturing Patent Rights as of the Effective Date are set forth on Schedule 1.8 attached hereto.

1.9 "**Akcea Patent Rights**" means, collectively, the Akcea Core Technology Patent Rights, the Akcea Manufacturing Patent Rights and the Akcea Product-Specific Patent Rights.

1.10 "**Akcea Product Positioning and Branding Strategy**" means Akcea's positioning and branding strategy for a Product.

1.11 "**Akcea Product-Specific IP**" means the Akcea Product-Specific Know-How and the Akcea Product-Specific Patent Rights.

1.12 "**Akcea Product-Specific Know-How**" means all Know-How Controlled by Akcea or its Affiliates on the Effective Date or at any time during the Term necessary to Develop or Commercialize a Product or disclosed by Akcea to PTC and, in each case specifically relates to (a) the composition of matter of a Product or (b) methods of using a Product as a prophylactic or therapeutic; *provided*, *however*, Know-How Controlled by Akcea or any of its Affiliates that (i) consists of subject matter applicable to oligonucleotide compounds or products in general or (ii) relates to an oligonucleotide compound that does not specifically modulate expression of a Target via the binding, partially or wholly, of such compound to RNA that encodes a Target, will not be considered Akcea Product-Specific Know-How, and in the case of (i) and (ii), such Know-How will be considered Akcea Core Technology Know-How.

1.13 "**Akcea Product-Specific Patent Rights**" means all Patent Rights Controlled by Akcea or its Affiliates on the Effective Date or at any time during the Term Covering (a) the composition of matter of a Product, (b) methods of using a Product, or (c) an oligonucleotide compound that specifically modulates expression of a Target via the binding, partially or wholly, of such compound to RNA that encodes a Target; *provided*, *however*, that Patent Rights Controlled by Akcea or any of its Affiliates to the extent that such Patent Rights include any claims that are directed to (i) subject matter applicable to oligonucleotide compounds or products in general or (ii) an oligonucleotide compound that does not specifically modulate expression of a Target via the binding, partially or wholly, of such compound to RNA that encodes a Target, will not be considered Akcea Product-Specific Patents, and in the case of (i) and (ii), such claims in such Patent Rights will be considered Akcea Core Technology Patents. The Akcea Product-Specific Patent Rights as of the Effective Date are set forth on Schedule 1.13 attached hereto.

1.14 "**Akcea Territory**" means the entire world, excluding the PTC Territory.

1.15 "**AKCEA-TTR-L_{Rx}**" means:

1. the compound known as AKCEA 682884 having the following sequence and chemistry: [**]; and/or

(ii) any oligonucleotide compound (other than [**] and [**]) designed to modulate expression of TTR via the binding, partially or wholly, of such compound to the RNA that encodes TTR, that is determined after [**] (but prior to the [**]) by Ionis Pharmaceuticals' research management committee as ready to start the pharmacokinetic and toxicology studies required to meet the requirements for filing an IND.

1.16 "**AKCEA-TTR-L_{Rx} Pivotal Clinical Trial**" means the first Phase 3 Clinical Trial (or the first clinical study that is intended to be a pivotal clinical study and on the basis of which Regulatory Approval Application would be filed) conducted by Ionis Pharmaceuticals and/or Akcea in accordance with the applicable Ionis Pharmaceuticals/Akcea License Agreement, as further described on Schedule 1.16 attached hereto.

1.17 "**ANVISA**" means the Brazilian Health Regulatory Agency (Agência Nacional de Vigilância Sanitária) and any successor entity with similar responsibility thereto.

1.18 "**API**" means the bulk active pharmaceutical ingredient manufactured in accordance with cGMP (unless expressly stated otherwise) for a Product. The quantity of API will be the as-is gross mass of the API after lyophilization (i.e., including such amounts of water, impurities, salt, heavy metals, etc. within the limits set forth in the API specifications).

1.19 **"APOC3"** means the gene target apolipoprotein C3 (GenBank accession # NM_000040; Gene ID: 345) or any alternative splice variants, mutants, polymorphisms and fragments thereof.

1.20 "**Business Day**" means any day, other than Saturday, Sunday, or any statutory holiday or bank holiday in the United States.

1.21 "**Calendar Quarter**" means a period of three (3) consecutive months ending on the last day of March, June, September, or December, respectively.

1.22 "**Calendar Year**" means a period of twelve (12) consecutive months beginning on January 1 and ending on December 31.

1.23 "**Change of Control**" means, with respect to a Party (a) the acquisition of beneficial ownership, directly or indirectly, by any Third Party of securities or other voting interest of such Party representing a majority or more of the combined voting power of such Party's then outstanding securities or other voting interests, (b) any merger, reorganization, consolidation or business combination involving such Party with a Third Party that results in the holders of beneficial ownership (other than by virtue of obtaining irrevocable proxies) of the voting securities or other voting interests of such Party (or, if applicable, the ultimate parent of such Party) immediately prior to such merger, reorganization, consolidation or business combination ceasing to hold beneficial ownership of more than fifty percent (50%) of the combined voting power of the surviving entity immediately after such merger, reorganization, consolidation or business combination, or (c) any sale, lease, exchange, contribution or other transfer to a Third Party (in one transaction or a series of related transactions) of all or substantially all of the assets of such Party to which this Agreement relates. The acquiring or combining Third Party in any of clause (a), (b) or (c), is referred to herein as the "**Acquirer**".

1.24 "**Clinical Trial**" means a Phase 1 Clinical Trial, Phase 2 Clinical Trial, Phase 3 Clinical Trial or any other study in which human subjects or patients are dosed with a drug, whether approved or investigational, including, for the avoidance of doubt, the AKCEA-TTR-L_{Rx} Pivotal Clinical Trial.

1.25 "**Commercialization**" and "**Commercialize**" means any and all activities undertaken relating to the marketing, obtaining pricing and reimbursement approvals, post-marketing commitments, promotion (including advertising, detailing or continuing medical education), any other offering for sale or any sale of a product, including any distribution, importation, exportation or transport of a product for sales purposes. "Commercialization" shall not include Development or Manufacturing.

1.26 "**Commercially Reasonable Efforts**" means, with respect to the efforts to be expended by a Party with respect to an agreed objective, such reasonable, diligent, and good faith efforts as such Party would normally use to accomplish a similar objective for its own internally developed product that is of similar market potential at a similar stage in its Development, Commercialization or product life, taking into account all relevant factors, including (a) the potential profitability of the product, (b) the costs and risks of Developing, Manufacturing, having Manufactured, using and Commercializing the product, (c) scientific, safety and regulatory concerns, (d) product profile, (e) the competitiveness of the marketplace and (f) the proprietary position of the product. "*Commercially Reasonable Efforts*" shall be determined on a country-by-country or market-by-market basis (as most applicable) for a particular product, and it is anticipated that the level of effort will change over time, including to reflect changes in the status of the product and the countries (or markets) involved. For the avoidance of doubt, where a Party has an obligation to use Commercially Reasonable Efforts, the efforts of such Party and its Affiliates, subcontractors and Sublicensees shall be considered in determining whether such Party has satisfied such obligation.

1.27 "**Comparable Third Party Product**" means, with respect to a Product in any country in the PTC Territory, any pharmaceutical product sold by a Third Party not authorized by or on behalf of PTC, its Affiliates or Sublicensees in such a country, that:

(a) contains, as an active pharmaceutical ingredient, the same compound as the Compound contained in the applicable Product; and

(b) is approved by the applicable Regulatory Authority for sale in such country.

1.28 "**Comparable Third Party Product Competition**" means, with respect to a Product in any country in the PTC Territory in a given Calendar Quarter, that, during such Calendar Quarter:

(a) one or more Comparable Third Party Product(s) is commercially available in such country; and

(b) such Comparable Third Party Product(s) have a market share of [**] percent ([**]%) or more of the aggregate market in such country of such Product and the Comparable Third Party Product(s) (based on sales of units of such Product and such Comparable Third Party Product(s), as reported by IMS International, or if such data are not available, such other reliable data source as reasonably agreed by the Parties in writing).

1.29 "**Compound**" means any of inotersen or volanesorsen.

1.30 "**Compounds**" means inotersen and volanesorsen.

1.31 "**Conjugate Technology**" means chemistry designed to enhance targeting or uptake of antisense drugs to specific tissues and cells. Conjugate Technology includes N-acetylgalactosamine (GalNAc) ligand conjugates capable of binding to the asialoglycoprotein receptor (ASGP-R) and enhancing the targeting or uptake of antisense drugs to the liver.

1.32 "**Control**" or "**Controlled**" means possession of the ability to grant a license or sublicense hereunder without violating the terms of any agreement with any Third Party (or Ionis with respect to the rights obtained from Ionis under the Ionis Pharmaceuticals/Akcea License Agreements); *provided, however*, that if a Party has a right to grant a license or sublicense with respect to an item of intellectual property to the other Party only upon payment of compensation (including milestones or royalties) to a Third Party, then the first Party will be deemed to have "*Control*" of the relevant item of intellectual property only if the other Party agrees to bear such compensation owed to such Third Party. For purposes of clarity, the foregoing proviso shall not apply to Ionis Pharmaceuticals or to payments made by Akcea to Ionis Pharmaceuticals under the Ionis Pharmaceuticals/Akcea License Agreement. Notwithstanding anything to the contrary under this Agreement, with respect to any Third Party that later becomes an Affiliate of Akcea after the Effective Date (including a Third Party acquirer), no intellectual property of such Third Party will be included in the licenses granted hereunder by virtue of such Third Party becoming an Affiliate of Akcea, except to the extent that intellectual property of such Affiliate is utilized by Akcea in the Development, Manufacture or Commercialization of Products.

1.33 "**Cover**" or "**Covered**" or "**Covering**" means, with respect to a Patent Right and a Product, that, but for rights granted to a Person under such Patent Right the act of making, using, or selling of such Product by such Person would infringe a Valid Claim included in such Patent Right, or in the case of a Patent Right that is a patent application, would infringe a Valid Claim in such patent application if it were to issue as a patent. If Akcea assigns an Akcea Product-Specific Patent Right to PTC, then such Patent Right will still be considered an Akcea Product-Specific Patent Right hereunder and a Product will be deemed "*Covered*" by such Akcea Product-Specific Patent Right for purposes of this Agreement.

1.34 "**Develop**" or "**Development**" means clinical research and development activities commencing with IND-enabling studies, including drug metabolism and pharmacokinetics, translational research, toxicology, pharmacology toxicology studies, statistical analysis and report writing, formulation development and optimization, Clinical Trials, regulatory affairs (including preparation for a Regulatory Approval Application submission and other submission-related activities), product approval and registration activities, and all other activities necessary to conduct IND-enabling studies or seek, obtain and maintain Regulatory Approval. "Development" shall not include Commercialization or Manufacturing.

1.35 "**Dollars**" or "**$**" means the legal tender of the U.S.

1.36 "**Drug Product**" means any drug product containing API as an active ingredient in finished bulk form or in packaged and labeled form.

1.37 "**EMA**" means the European Medicines Agency, and any successor entity thereto.

1.38 "**Executive Officers**" means the President, or his or her designee, in the case of Akcea, and the Chief Operating Officer, or his or her designee, in the case of PTC.

1.39 "**Existing In-License Agreements**" means the Ionis Pharmaceuticals/Akcea License Agreements and those other Akcea in-licenses set forth on Schedule 1.39 attached hereto.

1.40 "**Exploit**" or "**Exploitation**" means to make, have made, import, use, sell, or offer for sale, Develop, Manufacture or Commercialize.

1.41 "**FDA**" means the U.S. Food and Drug Administration, and any successor entity thereto.

1.42 "**First Commercial Sale**" means, with respect to a Product, the first sale for which revenue has been recognized by PTC or its Affiliates or Sublicensees for use or consumption by the general public of such Product in any country in the PTC Territory for which all Regulatory Approvals and pricing or reimbursement approvals that are legally required in order to sell such Product in such country have been granted; in each case *provided however* that the following shall *not* constitute a First Commercial Sale:

(a) any sale to an Affiliate or Sublicensee unless the Affiliate or Sublicense is the last entity in the distribution chain of the Product;

(b) any use of such Product in Clinical Trials, non-clinical Development activities or other Development activities with respect to such Product by or on behalf of a Party, or disposal or transfer of such Product for a bona fide charitable purpose; and

(c) any transfer for non-clinical or clinical studies, patient-assistance programs, charitable donations or compassionate use purposes.

For clarity, a "*First Commercial Sale*" of a Product in a country may be made by PTC or its Affiliates or Sublicensees pursuant to any approvals that may be granted pursuant to any order, requirement, directive, decree, mandate, legal action or judicial process or other legal process of any court or other Governmental Authority of competent jurisdiction in any country in the PTC Territory.

1.43 "**Future In-License Agreement**" means any agreement between Akcea (or, subject to Section 15.3, any of its Affiliates), on the one hand, and a Third Party, on the other hand, pursuant to which Akcea or any of its Affiliates acquires Control

of any Know-How or Patent Right that would be Akcea IP.

1.44 "**Good Clinical Practices**" or "**cGCP**" means (a) the then-current standards, practices, procedures and regulatory requirements promulgated or endorsed by the FDA and its applicable foreign counterparts and (b) the guidelines adopted by the International Conference on Harmonization ("**ICH**"), titled "Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance" (or any successor document), as each may be updated from time to time.

1.45 "**Good Laboratory Practices**" or "**cGLP**" means the then-current good laboratory practice standards promulgated or endorsed by the FDA, as defined in U.S. 21 C.F.R. Part 58, and such comparable regulatory standards in those applicable jurisdictions outside of the United States.

1.46 "**Good Manufacturing Practices**" or "**cGMP**" means (a) the then-current good manufacturing practices and standards promulgated or endorsed by the FDA, as provided for in the Current Good Manufacturing Practice Regulations of the U.S. Code of Federal Regulations Title 21 (21 C.F.R. §§210 and 211), and such comparable regulatory standards in those applicable jurisdictions outside of the United States, and (b) the guidelines adopted by the ICH, titled, "*Good Manufacturing Practice Guide for Active Ingredients, Q7*".

1.47 "**Governmental Authority**" means any multinational, federal, national, state, provincial, local or other entity, office, commission, bureau, agency, political subdivision, instrumentality, branch, department, authority, board, court, arbitral or other tribunal exercising executive, judicial, legislative, police, regulatory, administrative or taxing authority or functions of any nature pertaining to government.

1.48 "**In-License Agreement**" means (a) any Existing In-License Agreement, and (b) any Future In-License Agreement; in each case of (a) and (b), as amended from time to time.

1.49 "**IND**" means an investigational new drug application submitted to the FDA pursuant to Part 312 of Title 21 of the U.S. Code of Federal Regulations, including any amendments thereto. References herein to IND shall include, to the extent applicable, any comparable filing(s) outside the U.S. for the investigation of any product in any other country or group of countries.

1.50 "**inotersen**" means the compound having the following sequence and chemistry: 5¢-^{Me}U^{Me}C^{Me}U^{Me}UGGTTA^{Me}CATGAAA^{Me}U^{Me}C^{Me}C^{Me}C- 3.¢ The underlined residues are 2'-O-(2-methoxyethyl) nucleosides (2'-MOE nucleosides). The residues are arranged so that there are five 2'-MOE nucleosides at the 5¢ and 3¢-ends of the molecule flanking a gap of ten 2¢-deoxynucleosides. The cytosine and uracil bases are methylated at the 5-position. ^{Me}U and T have the same nucleobase structure and the choice for the symbol depends on whether the sugar is 2′-deoxy-D-ribose or D-ribose. Each of the 19 internucleoside linkages is a phosphorothioate linkage. Inotersen does not include any product containing Conjugate Technology.

1.51 "**Invention**" or "**Invented**" means the result or act of invention as determined in accordance with US patent laws.

1.52 "**Ionis Pharmaceuticals/Akcea License Agreements**" means the following agreements: (a) the Development, Commercialization and License Agreement, dated as of December 18, 2015, between Ionis Pharmaceuticals (f/k/a Isis Pharmaceuticals, Inc.) and Akcea, as amended from time to time; and (b) the Development, Commercialization, Collaboration, and License Agreement, dated as of March 14, 2018, between Ionis Pharmaceuticals and Akcea, as amended from time to time.

1.53 "**Ionis Pharmaceuticals**" means Ionis Pharmaceuticals, Inc., a Delaware corporation, having its principal place of business at 2855 Gazelle Court, Carlsbad, CA 92010.

1.54 "**Know-How**" means all unpatented information, know-how and data, including trade secrets, inventions (whether patentable or not), discoveries, methods, specifications, processes, expertise, technology, other non-clinical, pre-clinical and clinical data, documentation and results (including pharmacological, toxicological, biological, chemical, physical, safety and manufacturing data and results), analytical and quality control data and results, Regulatory Filings and other technical information. "Know-How" excludes in any event any Patent Rights.

1.55 "**Law**" means any law, statute, rule, regulation, order, judgment or ordinance having the effect of law of any federal, national, multinational, state, provincial, county, city or other political subdivision.

1.56 "**Manufacture**" or "**Manufacturing**" means all activities related to the manufacturing of an active pharmaceutical ingredient or product, including test method development and stability testing, formulation, process development, manufacturing scale-up, manufacturing for use in non-clinical and clinical studies, manufacturing for commercial sale, packaging, release of product, quality assurance/quality control development, quality control testing (including in-process, in-process release and stability testing) and release of product or any component or ingredient thereof, and regulatory activities related to all of the foregoing. "Manufacturing" shall not include Development or Commercialization.

1.57 "**NDA**" means a New Drug Application (as more fully described in 21 C.F.R. 314.50 et seq. or its successor regulation) and all amendments and supplements thereto filed with the FDA, or any equivalent filing, in a country or regulatory jurisdiction other than the United States.

1.58 "**Net Sales**" means with respect to any Product, the gross amount invoiced by PTC, any of its Affiliates and or any Sublicensee (each, a "**Selling Party**") to a Third Party (including a customer, distributor, wholesaler or end user) for sales or distribution of such Product, less the following deductions as calculated in accordance with the applicable Accounting Standard as consistently applied:

1.58.1 normal trade, cash, quantity and other customary discounts actually given to customers in the ordinary course of business;

1.58.2 rebates, credits and allowances given by reason of rejections returns, damaged or defective product or recalls;

1.58.3 government-mandated rebates and any other compulsory payments, credits, adjustments and rebates actually paid or deducted;

1.58.4 [**] percent ([**]%) of all price adjustments, allowances, credits, chargeback payments, discounts, rebates, fees and reimbursements or similar payments granted or made to wholesalers, distributors or other trade customers (the "**Specific Discounts**"); *provided*, *however*, the total deduction allowed for such Specific Discounts shall be capped at [**] percent ([**]%) of the ex-factory sales price for the applicable Product;

1.58.5 price adjustments, allowances, credits, chargeback payments, discounts, rebates, free of charge concessions, fees and reimbursements or similar payments granted or made to managed care organizations, group purchasing organizations or other buying groups, pharmacy benefit management companies, health maintenance organizations and any other providers of health insurance coverage, health care organizations or other health care institutions (including hospitals), health care administrators, patient assistance or other similar programs, or to federal state/provincial, local and other governments, including their agencies (but in all cases excluding Specific Discounts, which shall solely be governed by the preceding subsection);

1.58.6 reasonable and customary freight, shipping, insurance and other transportation expenses, if actually borne by the applicable Selling Party without reimbursement from any Third Party; and

1.58.7 sales, value-added, excise taxes, tariffs and duties, and other taxes and government charges directly related to the sale, delivery or use of such Product (but not including taxes assessed against the net income derived from such sale.)

If non-monetary consideration is received for any Product, Net Sales will be calculated based on the average price charged for such Product during the preceding Calendar Quarter in the relevant country, or in the absence of such sales, the fair market value of the Product, as determined by the Parties in good faith.

Furthermore, Net Sales shall not include use or transfer of a Product free of charge by PTC, its Affiliates and/or its Sublicensees for non-clinical or clinical studies, patient-assistance programs, charitable donations or compassionate use.

Resales or sales of a Product made in good faith between or among PTC, any of its Affiliates or any Sublicensee shall not be included in the calculation of Net Sales as long as, with respect to such resales or sales, the first sale thereafter to a non-Sublicensee Third Party is included in the calculation of Net Sales.

PTC and Akcea agree that any reasonable definition of "Net Sales" customarily used in drug discovery, development or commercialization licensing or collaboration contracts that is agreed to by PTC (or an Acquirer or assignee) and a sublicensee with respect to royalties payable to PTC from such sublicensee in an arms-length transaction under a particular sublicense will replace the definition of Net Sales in this Agreement and will be used in calculating the royalty payment to Akcea on sales of Products sold pursuant to such sublicense and due under this Agreement, for so long as the same definition of net sales is used to calculate the royalty payable from the applicable sublicensee to PTC.

For the avoidance of doubt, and notwithstanding any provision to the contrary in this Agreement, sales of a Product made in connection with any order, requirement, directive, decree, mandate, legal action or judicial process or other legal process of any court or other Governmental Authority of competent jurisdiction in the PTC Territory shall be included in the calculation of Net Sales.

1.59 "**Patent Right**" means (a) patents, patent applications, and similar government-issued rights protecting inventions in any country or jurisdiction however denominated, (b) all priority applications, divisionals, continuations, substitutions, continuations-in-part of and similar applications claiming priority to any of the foregoing, and (c) all patents and similar government-issued rights protecting inventions issuing on any of the foregoing applications, together with all registrations, reissues, renewals, re-examinations, confirmations, supplementary protection certificates, and extensions of any of (a), (b), or (c).

1.60 "**Permitted Licenses**" means (1) licenses granted by Akcea or its Affiliates before or after the Effective Date to any Third Party under the Akcea Core Technology Patent Rights, the Akcea Manufacturing and Analytical Patent Rights, or the Akcea Manufacturing and Analytical Know-How (but not under the Akcea Product-Specific Patent Rights) to (a) use oligonucleotides (or supply oligonucleotides to end users) solely to conduct pre-clinical research, or (b) enable such Third Party to manufacture or

formulate oligonucleotides, where (i) such Third Party is primarily engaged in providing contract manufacturing or services and is not primarily engaged in drug discovery, development or commercialization of therapeutics; and (ii) neither Akcea nor its Affiliates assists such Third Party to identify, discover or make a Product; and (2) material transfer agreements with academic collaborators or non-profit institutions solely to conduct non-commercial research.

1.61 "**Permitted Sublicensee**" means any Third Party distributor, logistics provider or other Third Party providers in support of Manufacturing or Commercialization of Compounds and/or Products in the applicable Territory.

1.62 "**Person**" means any individual, partnership, joint venture, limited liability company, corporation, firm, trust, association, unincorporated organization, Governmental Authority, or any other entity not specifically listed in this Section 1.61.

1.63 "**Phase 1 Clinical Trial**" means a human clinical trial (or a portion of a human clinical trial) of a product in any country, the principal purpose of which is a preliminary determination of safety in healthy individuals or patients, that would satisfy the requirements of 21 C.F.R. 312.21(a), or a similar clinical study prescribed by the relevant Regulatory Authorities in a country other than the United States.

1.64 "**Phase 2 Clinical Trial**" means a human clinical trial (or a portion of a human clinical trial) of a product in any country that would satisfy the requirements of 21 C.F.R. 312.21(b) and whose design is intended to explore a variety of doses, dose response, and duration of effect, and to generate initial evidence of clinical safety and activity in a target patient population, or a similar clinical study prescribed by the relevant Regulatory Authorities in a country other than the United States.

1.65 "**Phase 3 Clinical Trial**" means a human clinical trial (or a portion of a human clinical trial) of a product in any country that would satisfy the requirements of 21 C.F.R. 312.21(c) and whose design is intended to (a) establish that the product is safe and efficacious for its intended use, (b) define warnings, precautions and adverse reactions that are associated with the product in the dosage range to be prescribed, and (c) support Regulatory Approval for such product.

1.66 "**Phase 4 Clinical Trial**" means a human clinical trial of a product that (a) is not required for receipt of Regulatory Approval for a country but which may be useful in providing additional drug profile data in support of such Regulatory Approval (whether the trial is commenced prior to or after receipt of such Regulatory Approval), or (b) is required, requested or advised by a Regulatory Authority as a condition of, or in connection with, obtaining or maintaining a Regulatory Approval (whether the trial is commenced prior to or after receipt of such Regulatory Approval). Phase 4 Clinical Trials may include trials or studies conducted in support of pricing/reimbursement, epidemiological studies, modeling and pharmacoeconomic studies, post-marketing surveillance studies, investigator sponsored clinical trials and health economics studies.

1.67 "**Prior Agreements**" means the agreements listed on Schedule 7.1.2 attached hereto.

1.68 "**Product**" means any product containing either (a) inotersen, or (b) volanesorsen, in each case in their forms as they exist on the Effective Date, alone or in combination with one or more other active ingredients in any and all dosage forms and strengths and delivery modes. For the avoidance of doubt, AKCEA-TTR-L_{Rx} is not a "*Product*" under this Agreement.

1.69 "**Prosecution and Maintenance**" or "**Prosecute and Maintain**" means, with regard to a Patent Right, the preparation, filing, prosecution and maintenance of such Patent Right, as well as re-examinations, reissues, appeals, and requests for patent term adjustments and patent term extensions with respect to such Patent Right, together with the initiation or defense of interferences, the initiation or defense of oppositions and other similar proceedings with respect to the particular Patent Right, and any appeals therefrom. For clarification, "Prosecution and Maintenance" or "Prosecute and Maintain" shall not include any other enforcement actions taken with respect to a Patent Right.

1.70 "**PTC Background Know-How**" means Know-How that is (a) Controlled by PTC on the Effective Date or thereafter during the Term, (b) arises outside of the activities conducted under this Agreement, (c) is disclosed or used by PTC in connection with the conduct of the Exploitation of Compounds or Products hereunder, and (d) is necessary or reasonably useful for the Exploitation of Compounds or Products in the PTC Territory.

1.71 "**PTC Background Patent Rights**" means those Patent Rights Controlled by PTC or any of its Affiliates on the Effective Date or thereafter during the Term that Cover PTC Background Know-How.

1.72 "**PTC IP**" means the PTC Background Know-How, the PTC Background Patent Rights, the PTC Product-Specific Patent Rights and the PTC Product-Specific Know-How.

1.73 "**PTC Patent Rights**" means the PTC Background Patent Rights and the PTC Product-Specific Patent Rights.

1.74 "**PTC Product-Specific IP**" means the PTC Product-Specific Know-How and the PTC Product-Specific Patent Rights.

1.75 "**PTC Product-Specific Know-How**" means all Know-How Controlled by PTC or its Affiliates on the Effective Date or at any time during the Term necessary to Develop or Commercialize a Product or disclosed by Akcea to PTC and, in each case, specifically relates to (a) the composition of matter of a Product or (b) methods of using a Product as a prophylactic or

therapeutic; *provided*, *however*, Know-How Controlled by PTC or any of its Affiliates that (i) consists of subject matter applicable to oligonucleotide compounds or products in general or (ii) relates to an oligonucleotide compound that does not specifically modulate expression of a Target via the binding, partially or wholly, of such compound to RNA that encodes a Target, will not be considered PTC Product-Specific Know-How.

1.76 "**PTC Product-Specific Patent Rights**" means all Patent Rights Controlled by PTC or its Affiliates on the Effective Date or at any time during the Term Covering (a) the composition of matter of a Product, (b) methods of using a Product, or (c) an oligonucleotide compound that specifically modulates expression of a Target via the binding, partially or wholly, of such compound to RNA that encodes a Target; *provided*, *however*, that Patent Rights Controlled by PTC or any of its Affiliates to the extent that such Patent Rights include any claims that are directed to (i) subject matter applicable to oligonucleotide compounds or products in general or (ii) an oligonucleotide compound that does not specifically modulate expression of a Target via the binding, partially or wholly, of such compound to RNA that encodes a Target, will not be considered PTC Product-Specific Patent Rights..

1.77 "**PTC Territory**" means Latin America and the Caribbean, using the United Nations M49 standard definition for that region, *but excluding* the following countries and territories: Anguilla, Aruba, Bahamas, Barbados, Bonaire, Sint Eustatius and Saba, British Virgin Islands, Cayman Islands, Curaçao, Guadeloupe, Martinique, Montserrat, Puerto Rico, Saint Barthélemy, Saint Martin (French Part), Sint Maarten (Dutch part), Turks and Caicos Islands, United States Virgin Islands, Bouvet Island, Falkland Islands (Malvinas), French Guiana, South Georgia and the South Sandwich Islands.

1.78 "**Regulatory Approval**" means the approval of the applicable Regulatory Authority necessary for the marketing and sale of a product in a given country, excluding any pricing and reimbursement approvals that may be required, and including the expansion or modification of the label for additional indications or uses.

1.79 "**Regulatory Approval Application**" means (a) an NDA, or (b) any other application to seek Regulatory Approval of a product in any country, as defined in applicable Laws and filed with the relevant Regulatory Authorities of such country.

1.80 "**Regulatory Authority**" means the FDA in the United States, ANVISA in Brazil or any Governmental Authority in another country in the Territory that holds responsibility for granting Regulatory Approval for a product in such country and any successor(s) thereto.

1.81 "**Regulatory Exclusivity**" means any exclusive marketing rights or data exclusivity rights conferred by any Regulatory Authority with respect to any Product that precludes the use of any clinical data collected and filed for such Product for the benefit of any Regulatory Approval for a generic or biosimilar product (for any use), including orphan or pediatric exclusivity where applicable.

1.82 "**Regulatory Filing**" means, with respect to a product, any documentation comprising or relating to or supporting any filing or application with any Regulatory Authority with respect to such product, or its use or potential use, including any document submitted to any Regulatory Authority, including any IND, any drug master files, any Regulatory Approval Application and any correspondence with any Regulatory Authority with respect to such product (including minutes of any meetings, telephone conferences or discussions with any Regulatory Authority).

1.83 "**Royalty Trigger Date**" means, on a Product-by-Product basis, the earlier to occur with respect to a Product of (a) the date that is twelve (12) months after the First Commercial Sale of such Product in Brazil; or (b) the date in which PTC or its Affiliates or Sublicensees have recognized revenue of ten million U.S. Dollars ($10,000,000) or more in cumulative Net Sales of such Product in the PTC Territory.

1.84 "**Target**" means (a) in the case of inotersen, TTR; and (b) in the case of volanesorsen, APOC3.

1.85 "**Territory**" means, as the context requires, either (a) the PTC Territory or the Akcea Territory, or (b) the PTC Territory and the Akcea Territory together.

1.86 "**Third Party**" means any Person that is neither a Party nor an Affiliate of a Party.

1.87 "**Trademark**" means trademarks, service marks, certification marks, trade dress, internet domain names, trade names, identifying symbols, designs, product names, company names, slogans, logos or insignia, whether registered or unregistered, and all common law rights, applications and registrations therefor, and all goodwill associated therewith.

1.88 "**TTR**" means the gene target, transthyretin (GenBank accession # NM_000371; Gene ID: 7276), or any alternative splice variants, mutants, polymorphisms, and fragments thereof.

1.89 "**United States**" or "**U.S.**" means the United States of America and all of its territories and possessions.

1.90 "**Valid Claim**" means a claim of a Patent Right that (a) in the case of any granted, unexpired United States Patent Right or foreign Patent Right, will not have been donated to the public, disclaimed, or held invalid or unenforceable by a court of competent jurisdiction in an unappealed or unappealable decision, or (b) in the case of any United States or foreign patent application, is being prosecuted in good faith and will not have been permanently cancelled, withdrawn, or abandoned, provided

that (i) no more than [**] years have passed since the earliest date of filing for such application in the United States (unless and until such claim is granted), and (ii) no more than [**] years have passed since the earliest date of filing for such application outside of the United States (unless and until such claim is granted).

1.91 "**volanesorsen**" means the compound known as ISIS 304801 having the following sequence and chemistry: 5′-AG^{Me}C^{Me}U^{Me}U^{Me}CTTGT^{Me}C^{Me}CAG^{Me}C^{Me}U^{Me}U^{Me}UA^{Me}U-3′. The underlined residues are 2'-O-(2-methoxyethyl) nucleosides (2'-MOE nucleosides). The residues are arranged so that there are five 2'-MOE nucleosides at the 5' and 3' ends of the molecule flanking a gap of ten 2'-deoxynucleosides. The cytosine and uracil bases are methylated at the 5-position. Each of the 19 internucleoside linkages is a phosphorothioate diester linkage. Volanesorsen does not include any product containing Conjugate Technology.

1.92 Additional Definitions. Each of the following definitions is set forth in the section of this Agreement indicated below:

Definition:	**Section:**
Acquirer	1.23
Acquired Third Party	15.3.4
Agreement	Preamble
Akcea	Preamble
Akcea Core Technology Patent Rights	10.1.3
Akcea Indemnified Parties	13.1
Akcea Invention	10.1.2
Akcea-Owned Categories	10.1.3
Akcea Proposed Transaction Entity	7.2.4
Alliance Manager	5.5
CMO	4.1
Committee	5.2.1
Competitive Infringement	10.3.1
Compulsory Third Party Product	9.5.
Confidential Information	11.1
Cross-Territory Sales	3.10.2
Cross-Territory Sales Notice	3.10.2
Cross-Territory Sales Report	3.10.3
Defense Proceeding	10.2.1(a)
Disclosing Party	11.1
Dispute	15.2
Distributing Party	3.10.2
eCTD	2.5.3
Effective Date	Preamble
Evaluation Package	7.2.1
Exclusive License	6.1.1
Existing Confidentiality Agreement	11.1.4
Expiration of the ROFN Right	7.2.1
Final Offer	7.2.3(b)
FPL	7.1
GAAP	15.13
ICH	1.41
Inbound Licensor	6.2.1
Incremental Tax Cost	15.3.1
Indemnified Party	13.3
Indemnifying Party	13.3
Initial Fee	9.1
Inotersen Buy-Out	7.2.3(a)
Inotersen Buy-Out Option	7.2.3
Inotersen FMV	7.2.3(a)
Ionis Internal ASO Safety Database	3.9.3
Ionis Pharmaceuticals/Akcea Product Regulatory Strategy	2.4.1
JAMS	15.2

Joint Invention	10.1.2
JSC	5.1.1
JSC Evaluation Presentation	7.2.1
Losses	13.1
Market Share Loss Percentage	9.5
Milestone Payment	9.2
Non-Exclusive License	6.1.2
Parties	Preamble
Party	Preamble
Pre-Existing Affiliates	15.3.3
Product Regulatory Strategy	2.4.2
Product Trademark	3.7.1
Promotional Materials	3.5
Proposed Transaction	7.2.1
PTC	Preamble
PTC Commercialization Plan	3.2
PTC Commercialization Targets	3.2
PTC Indemnified Parties	13.2
PTC Invention	10.1.2
PTC Parent	Recitals
Receiving Party	11.1
ROFN Right	7.2.1
Royalty Rate	9.3
Royalty Term	9.4
Securities Acts	11.3.3
SDEA	3.9.2
Selected Final Offer	7.2.3(c)
Selling Party	1.58
Specific Discounts	1.58.4
Subcommittee	5.2
Sublicense	6.4
Sublicensee	6.4
Supply Agreement	4.1
Term	14.1
Third Party Claims	13.1
Valuation Expert	7.2.3(b)
Valuation Notice	7.2.3(b)

ARTICLE 2
DEVELOPMENT; REGULATORY STRATEGY; KNOW-HOW TRANSFER

2.1 Product Development.

2.1.1 As between Akcea and PTC, in the Akcea Territory, Akcea is solely responsible for the Development activities relating to the Products and AKCEA-TTR-L_{Rx} in accordance with the terms of the Ionis Pharmaceuticals/Akcea License Agreements, the Strategic Plans and Transition Plans (each as defined therein) and any Regulatory (as defined therein) strategies contemplated under the Ionis Pharmaceuticals/Akcea License Agreements. As between Akcea and PTC, all costs and expenses incurred by or on behalf of Akcea in the performance of such Development activities shall be borne solely by Akcea.

2.1.2 Akcea shall promptly notify PTC (but in any case within [**]) of any Material Changes (as defined in the Ionis Pharmaceuticals/Akcea License Agreements) to the Strategic Plans and any material changes to the Transition Plans that have been approved pursuant to the Ionis Pharmaceuticals/Akcea License Agreements that may affect the Development of the Products in the PTC Territory.

2.1.3 Akcea shall consult with PTC in good faith regarding (a) the conduct and implementation of Akcea's activities under the Strategic Plans and the Transition Plans relating to the Development of the Products in the PTC Territory, and (b) any Material Change (as defined in the Ionis Pharmaceutical/Akcea License Agreements) prior to their implementation. If any such activities are solely related to the Development of the Products in the PTC Territory, then the Parties will mutually agree to a budget for such activities, and the costs of such activities under such mutually agreed budget will be borne by PTC.

2.1.4 Akcea shall invite PTC to appoint a representative to attend, and such PTC representative shall be permitted to attend, any portions of any JSC or other Subcommittee meetings that are held pursuant to the Ionis Pharmaceuticals/Akcea License Agreements that relate to the Development of any of the Products in the PTC Territory.

2.1.5 PTC will conduct any Phase 4 Clinical Trials that are required or requested in writing by a Regulatory Authority in a country in the PTC Territory as a condition of, or in connection with, obtaining or maintaining Regulatory Approval in such country (whether such Phase 4 Clinical Trial is commenced prior to or after receipt of such Regulatory Approval) or as otherwise determined by PTC to conduct. As between Akcea and PTC, all costs and expenses incurred by or on behalf of PTC in the performance of any such Phase 4 Clinical Trials shall be borne solely by PTC.

2.2 Akcea Progress Reports on Development Activities. PTC shall reasonably assist Akcea with the preparation of any progress updates to be provided to Ionis Pharmaceuticals with respect to the Development of the Products in the PTC Territory as required under the Ionis Pharmaceuticals/Akcea License Agreements. Akcea shall provide to the JSC a progress update regarding any regulatory activities related to a Product that occurred since the last update provided by Akcea to the JSC, including as to timing of obtaining Regulatory Approval for a Product in any country and any events that have occurred or information that has been obtained by Ionis Pharmaceuticals or Akcea relevant to the timing or the likelihood of obtaining Regulatory Approval in any country.

2.3 PTC Progress Reports on Regulatory Activities. PTC shall provide to the JSC a progress update regarding any regulatory activities related to a Product that occurred since the last update provided by PTC to the JSC, including as to timing of obtaining Regulatory Approval for a Product in any country and any events that have occurred or information that has been obtained by PTC relevant to the timing or the likelihood of obtaining Regulatory Approval in any country in the PTC Territory.

2.4 Regulatory Strategy.

2.4.1 All detailed plans for coordination and preparation of Regulatory Filings and Regulatory Approval Applications for market approval for the Products that have been agreed to by Ionis Pharmaceuticals and Akcea pursuant to the Ionis Pharmaceuticals/Akcea License Agreements as of the Effective Date have been disclosed by Akcea to PTC in writing or via the electronic data room hosted in connection with the transactions contemplated hereunder (the "**Ionis Pharmaceuticals/Akcea Product Regulatory Strategy**"). After the Effective Date, except to the extent required by a Regulatory Authority in a country in the Akcea Territory or as set forth in Section 2.4.2, Akcea may not make any changes to the Ionis Pharmaceuticals/Akcea Product Regulatory Strategy that would have a material adverse effect on the timing or likelihood of obtaining Regulatory Approval in a country in the PTC Territory.

2.4.2 The Parties shall cooperate in good faith to develop a written regulatory strategy for each Product in the PTC Territory for review and approval by the JSC (each, a "**Product Regulatory Strategy**"). Each Product Regulatory Strategy shall address (a) the activities and the allocation between the Parties of the pre-launch activities to be undertaken by each Party in preparation for the commercial launch of a Product in any country within the PTC Territory; (b) the timeline for the transition of any regulatory responsibilities (including, subject to Section 3.4, pricing and reimbursement approval responsibilities) by Akcea and/or Ionis Pharmaceuticals and their applicable Affiliates to PTC; and (c) the timeline for the assignment and transfer of all Regulatory Approvals, Regulatory Filings and/or any pricing and reimbursement approvals, held by Akcea and/or Ionis Pharmaceuticals with respect to any country in the PTC Territory to PTC in accordance with Section 2.5. By [**] of each Calendar Year, the Parties shall submit an updated version of the Product Regulatory Strategy for such Calendar Year to the JSC for review and approval. Once the JSC has approved a Product Regulatory Strategy, each Party will use Commercially Reasonable Efforts to execute its respective tasks and responsibilities within the time frames set forth in such Product Regulatory Strategy. Each Party will bear its own costs and expenses associated with any activities that such Party performs in support of the implementation of such Product Regulatory Strategy.

2.5 Transfer of Regulatory Filings and Regulatory Approvals.

2.5.1 Within thirty (30) days after the Effective Date, Akcea shall, with respect to each country in the PTC Territory, assign and transfer to PTC the ownership and sponsorship of such Regulatory Approval and any pricing and reimbursement approvals held in its or any of its Affiliate's or sublicensee's name in such country, to the extent any exist and to the extent consistent with applicable Law, and provide PTC with copies of all Regulatory Filings relating to the Products in the PTC Territory, including all reports, correspondence and conversation logs and all pre-clinical and clinical data and results related thereto. Thereafter, PTC shall prepare, file and maintain all Regulatory Filings and Regulatory Approvals for the applicable Product in such country. Akcea shall further appoint, and ensure that Ionis Pharmaceuticals and its other Affiliates and sublicensees appoint, PTC as their agent for all matters relating to such Products and Compounds involving Regulatory Authorities in the PTC Territory until all Regulatory Approvals, Regulatory Filings, and any pricing and reimbursement approvals held in its or its Affiliate's or sublicensee's name have been transferred to PTC. In addition, Akcea shall ensure that PTC shall have access to all data contained or referenced in Regulatory Approvals and Regulatory Filings in the Akcea Territory that are reasonably necessary for the Exploitation of the Compounds and the Products in the PTC Territory.

2.5.2 Each Party shall own and maintain in its possession all Regulatory Filings and Regulatory Approvals for the Products in its respective Territory.

2.5.3 In addition, within thirty (30) days after the Effective Date, Akcea shall provide to PTC a copy in an appropriate electronic format of all sections of the electronic common technical document ("**eCTD**") modules that relate to each of the Products in the Territory that have been agreed to by Akcea and Ionis Pharmaceuticals pursuant to the Ionis Pharmaceuticals/Akcea License Agreements. PTC may use such eCTD to obtain Regulatory Approvals for the Products in the PTC Territory.

2.6 Interactions with Regulatory Authorities.

2.6.1 After the Effective Date, PTC shall be responsible for, and shall take the lead with respect to, all meetings, communications and other interactions with all of the Regulatory Authorities in the PTC Territory, and will deliver, or cause to be delivered, to Akcea for its review copies of all documents and communications received from Regulatory Authorities in the PTC Territory, and, to the extent practicable under the relevant circumstances (*e.g.*, accelerated timeframes for responses or impromptu calls by regulators) will provide Akcea with a reasonable opportunity to review and comment on any such communications and related materials received by or to be submitted to any such Regulatory Authority (and PTC will not unreasonably refuse to implement any reasonable suggestions made by Akcea to such communications or materials). To the extent practicable under the relevant circumstances, Akcea (or, at Akcea's request, Ionis Pharmaceuticals) will have the right to attend, and PTC will provide Akcea with written notice of and an invitation to, any meeting PTC has formally scheduled or has definitive plans to hold with a Regulatory Authority relating to a Product in the PTC Territory; *provided*, *however*, that should Akcea be unable to attend a meeting, PTC will provide a summary of the meeting reasonably promptly thereafter. Following the first meeting with a Regulatory Authority attended by Akcea or Ionis (which Akcea and Ionis will bear its own costs to attend), PTC will reimburse Akcea's and Ionis' reasonable travel costs associated with such attendance at any such meetings with Regulatory Authorities if Akcea or Ionis declined to attend such meeting after being provided notice by PTC and either (i) PTC indicated PTC would like Akcea and/or Ionis to attend nonetheless, or (ii) a Regulatory Authority formally requires Akcea or Ionis to attend such meeting.

2.6.2 As soon as reasonably practicable, Akcea will deliver, or cause to be delivered, to PTC for its review copies of all important documents and communications received from Regulatory Authorities in Major Market (as defined in the Ionis Pharmaceuticals/Akcea License Agreements) countries that impact the Development and Commercialization of any of the Products in the PTC Territory.

2.7 Technology Transfer. Akcea will promptly deliver, or cause to be delivered, to PTC or one or more of PTC's designated Affiliates copies of all Know-How in Akcea's and Ionis Pharmaceutical's possession related to the Products in the PTC Territory that has not previously been provided to PTC for use solely in accordance with the licenses granted to PTC under Section 6.1.

2.8 Conversion of NEURO-TTR OLE Study. As soon as reasonably practicable, Akcea will use Commercially Reasonable Efforts to coordinate with PTC to convert all patients in the PTC Territory in the Phase 3 NEURO-TTR OLE study to a Phase 4 Clinical Trial, and PTC will use Commercially Reasonable Efforts to conduct such Phase 4 Clinical Trial, will be responsible for all costs related to such Phase 4 Clinical Trial in the PTC Territory, and PTC will not administer, or permit the administration of, inotersen in such Phase 4 Clinical Trial without a mutually agreed patient monitoring plan. PTC will also assume responsibility for the planning, conduct and expense of any new investigator-initiated studies or post-approval studies in the PTC Territory (*e.g.*, Phase 4 Clinical Trial) mutually agreed to by the Parties. Akcea shall remain responsible for all [**] related to the Phase 3 NEURO-TTR OLE study through [**], after which, *provided that* Akcea has used Commercially Reasonable Efforts to coordinate with PTC to convert all patients in the PTC Territory in the Phase 3 NEURO-TTR OLE study to a Phase 4 Clinical Trial, PTC will be solely responsible for such [**] in the PTC Territory; *provided, further, however*, that if, by [**], PTC is unable to convert all patients in the PTC Territory in the Phase 3 NEURO-TTR OLE study to a Phase 4 Clinical Trial due to a delay caused by ANVISA, then the Parties will [**] the obligation to [**] in the PTC Territory until the earlier of (i) the conclusion of such delay, and (ii) [**], after which time PTC will be solely responsible for such [**] in the PTC Territory.

2.9 Class Generic Claims for Products. To the extent PTC intends to make any claims in a Product label or regulatory filing for a Product in the PTC Territory that are class generic to antisense oligonucleotides, Ionis' generation 2.0 or 2.5 chemistry platform(s), or Conjugate Technology, PTC will provide Akcea with such proposed claims for Akcea's review and will [**] for such class generic claims in such label or regulatory filing.

ARTICLE 3
COMMERCIALIZATION

3.1 Diligence. Subject to Akcea's compliance with Section 2.5, PTC shall be solely responsible for, and shall use Commercially Reasonable Efforts to, Commercialize the Product in the PTC Territory at its sole cost and expense, including the pursuit and maintenance of applicable Regulatory Approvals in the PTC Territory and Commercialization of the Products in accordance with the PTC Commercialization Plan. In accordance with the Ionis Pharmaceuticals/Akcea License Agreements, as between Akcea and PTC, Akcea shall be solely responsible for Commercializing the Products in the Akcea Territory at its sole cost and expense, including the pursuit and maintenance of applicable Regulatory Approvals in the Akcea Territory. Each Party shall be

solely responsible at its own cost and expense for the Commercialization of the Products in their respective Territory, including the conduct of any post-marketing commitments or studies.

3.2 PTC Commercialization Plan. Within [**] after the receipt of Regulatory Approval for a Product in the PTC Territory, and thereafter within [**] after [**] of each Calendar Year, PTC shall submit to the JSC a written plan that summarizes (a) the status of its Commercialization activities with respect to the Products conducted during the immediately prior Calendar Year, and (b) a list of high-level, specific performance targets for the then-current Calendar Year for each of the Products that are currently in Commercialization in the PTC Territory, for review and approval by the JSC (such performance targets, the "**PTC Commercialization Targets**" and each such plan, a "**PTC Commercialization Plan**"). The initial PTC Commercialization Plan will be mutually agreed to by the Parties within [**] after the Effective Date, and will include, among other important Commercial matters, (i) pre-launch, launch, and subsequent Commercialization activities for each Product (which may include, as appropriate at any given time based on the stage of Commercialization, market access strategy, messaging, branding, pricing, a regulatory plan, advertising, education, publication planning, marketing, compliance, and field force training), (ii) key decisions and timelines for Commercialization activities, (iii) key strategies and tactics for implementing those activities, and (iv) a safety section that includes a robust patient monitoring plan. In addition, at each meeting of the JSC, PTC will provide to the JSC a progress update on PTC's performance of activities related to each Product under the PTC Commercialization Plan (including an update regarding the progress of any named patient or other similar programs), which progress update may take the form of a PowerPoint presentation. For clarity, the performance targets set forth in a PTC Commercialization Plan [**]; *provided, however*, that if PTC fails to achieve a performance target then [**].

3.3 Patient Safety. For the avoidance of doubt, the Parties acknowledge and agree that, for each Product, PTC will not administer, or permit the administration of, such Product in the PTC Territory until the Parties have mutually agreed on the initial patient monitoring plan described in Section 3.2(iv).

3.4 Pricing and Reimbursement. Notwithstanding anything to the contrary set forth in this Agreement, PTC and its Affiliates and Sublicensees shall take the lead in, and be responsible for, all pricing and reimbursement approval proceedings, discount and rebate strategies and other economic arrangements relating to the Products in the PTC Territory. Akcea shall assist PTC in obtaining pricing and reimbursement approvals in the PTC Territory, including, if required by applicable Law, to submit any pricing and reimbursement approval applications or other Regulatory Filings in Akcea and/or Ionis Pharmaceuticals' name(s) as reasonably requested by PTC. For the avoidance of doubt, Akcea or Ionis Pharmaceuticals shall be responsible for all pricing and reimbursement approval proceedings, discount and rebate decisions and other economic arrangements relating to the Products in the Akcea Territory.

3.5 Advertising and Promotional Materials. PTC shall develop all sales, promotion and advertising materials relating to the Products ("**Promotional Materials**") for use in the PTC Territory, which shall be consistent with the Akcea Product Positioning and Branding Strategy and compliant with applicable Laws and the provisions of the applicable Regulatory Approvals. Akcea shall provide reasonably promptly after the Effective Date and thereafter on a regular basis from time to time marketing, commercialization, medical education, and medical information materials to be adapted by PTC for use in the PTC Territory, and Akcea shall have the right to review the adapted materials and any new materials developed by PTC to ensure that they are consistent in message and quality with the materials being used in the Akcea Territory (and PTC shall not unreasonably refuse to implement material comments or input that Akcea provides with regard to such materials). Akcea shall in good faith consider any comments or input that PTC may have with regard to adapting the Akcea Product Positioning and Branding Strategy for use in the PTC Territory. Copies of all Promotional Materials used by PTC in the PTC Territory will be archived by PTC in accordance with applicable local Law.

3.6 Packaging and Labeling. PTC and its Affiliates or Sublicensees shall be solely responsible for all finished packaging and labeling of the Product to be sold or otherwise distributed in the PTC Territory in accordance with the Akcea Product Positioning and Branding Strategy and specifications for the Product set forth in the applicable Supply Agreement and the Quality Agreement, at PTC's sole cost and expense.

3.7 Trademarks.

3.7.1 Trademarks. The trademark under which each Product shall be marketed in the PTC Territory shall be determined by the JSC (each a "**Product Trademark**"). To the extent possible, the same Trademark(s) will be used for the Commercialization of a Product throughout the Territory. PTC shall register the Product Trademarks in the PTC Territory, shall be the exclusive owner of the Product Trademarks in the PTC Territory and, subject to Section 14.3.7, shall take all such actions as are required to continue and maintain in full force and effect and defend in the PTC Territory the Product Trademarks and related registrations, in each case at its sole cost and expense. Akcea shall register the Product Trademarks in the Akcea Territory in its sole discretion, shall be the exclusive owner of the Product Trademarks in the Akcea Territory, and shall be responsible for the filing, prosecution, defense and maintenance before all trademark offices in the Akcea Territory of the Product Trademarks applicable to the Product, in each case at its sole cost and expense. The Parties shall reasonably consult with each other with respect to matters relating to the Product Trademarks. To the extent any Product Trademarks specific to the brand names TEGSEDI (for inotersen) and WAYLIVRA (for volanesorsen) are registered or are the subject of pending applications for registration by Akcea as of the Effective Date in the PTC Territory, Akcea will use commercially reasonable efforts to transition those registrations or applications to PTC pursuant to a mutually-agreed timeline, following which PTC will be responsible for the prosecution, defense and

maintenance before all trademark offices in the PTC Territory of such Product Trademarks, in each case at PTC's sole cost and expense. In addition, to the extent either Party uses Product-specific URLs, those URLs will be owned and maintained by the respective Party in that party's Territory, in each case at such Party's sole cost and expense, and to the extent any URLs specific to the brand names TEGSEDI (for inotersen) and WAYLIVRA (for volanesorsen) are owned by Akcea as of the Effective Date in the PTC Territory, Akcea will use commercially reasonable efforts to transition those URLs to PTC pursuant to a mutually-agreed timeline. The Parties shall reasonably consult with each other with respect to matters relating to Product-specific URLs.

3.7.2 Trademark Licenses. Subject to the terms and conditions of this Agreement, each Party hereby grants to the other Party a license to use the Product Trademarks for the packaging, marketing, sale and promotion of the applicable Product in accordance with the terms of this Agreement and with trademark usage guidelines to be developed by the JSC.

3.8 Patient Assistance Programs. PTC shall be solely responsible for the conduct of any expanded access, early access, free-of-charge and other programs with respect to the Products in the PTC Territory. PTC shall be responsible for ensuring that such programs shall be consistent with any global safety monitoring standards provided by Akcea to the JSC and approved by the JSC for use in the PTC Territory.

3.9 Adverse Event Reporting; Global Safety Database.

3.9.1 PTC shall be responsible for reporting all adverse drug experiences associated with the Products in the PTC Territory to applicable Regulatory Authorities. Akcea shall be responsible for reporting all adverse drug experiences associated with the Products in the Akcea Territory to applicable Regulatory Authorities. Akcea shall also be responsible for establishing, holding and maintaining the global safety database for the Compounds and the Products in the Territory.

3.9.2 Within [**] after the Effective Date, the Parties shall enter into a mutually-agreed safety data exchange agreement (the "**SDEA**"), which agreement shall provide for the exchange by the Parties of any information of which a Party becomes aware concerning any adverse event experienced by a subject or patient being administered any Product, whether or not such adverse event is determined to be attributable to any Compound or Product, including any such information received by either Party from any Third Party (subject to receipt of any required consents from such Third Party). It is understood that each Party and its Affiliates and licensees or sublicensees shall have the right to disclose such information if such disclosure is reasonably necessary to comply with applicable Laws as well as requirements of any applicable Regulatory Authority.

3.9.3 Ionis' Internal Antisense Safety Database.

(a) Ionis Pharmaceuticals maintains an internal database that includes information regarding the tolerability of its drug compounds, individually and as a class, including information discovered during pre-clinical and clinical development (the "**Ionis Internal ASO Safety Database**"). In an effort to maximize understanding of the safety profile and pharmacokinetics of Ionis' and Akcea's compounds, PTC will cooperate in connection with populating the Ionis Internal ASO Safety Database. To the extent collected by PTC and in the form in which PTC uses/stores such information for its own purposes, PTC will provide Akcea with information concerning toxicology, pharmacokinetics, safety pharmacology study(ies), serious adverse events and other safety information related to each Product as soon as practicable following the date such information is available to PTC (but not later than [**] after PTC's receipt of such information). In connection with any reported serious adverse event, PTC will provide Akcea all serious adverse event reports, including initial, interim, follow-up, amended, and final reports. In addition, with respect to a Product, PTC will provide Akcea with copies of Annual safety updates filed with each IND and the safety sections of any final Clinical Study reports within [**] following the date such information is filed or is available to PTC, as applicable. Furthermore, PTC will promptly provide Akcea with any supporting data and answer any follow-up questions reasonably requested by Akcea. All such information disclosed by PTC to Akcea will be PTC Confidential Information; *provided, however*, that such PTC Confidential Information may be disclosed (i) by Akcea to Ionis to satisfy Akcea's obligations to Ionis under the Ionis Pharmaceuticals/Akcea License Agreements, (ii) by Akcea and/or Ionis to Ionis' other partners if such information is regarding class generic properties of oligonucleotides, or (ii) to any Third Party, in each case, so long as Akcea or Ionis does not disclose the identity of a Product or PTC. PTC will deliver all such information to Akcea for the Ionis Internal ASO Safety Database to Akcea Therapeutics, Inc., 22 Boston Wharf Road, Boston, Massachusetts 02210, Attention: Chief Medical Officer (or to such other address/contact designated in writing by Akcea). PTC will also cause its Affiliates and Sublicensees to comply with this Section 3.9.3(a).

3.9.4 From time to time, Akcea and Ionis will utilize the information in the Ionis Internal ASO Safety Database to conduct analyses to keep Ionis and Akcea, and their respective partners, informed regarding class generic properties of ASOs, including with respect to safety. As such, if and when Ionis or Akcea identifies safety or other related issues that may be relevant to a Product (including any potential class-related toxicity), Akcea will promptly inform PTC of such issues and, if requested, provide the data supporting Akcea's conclusions.

3.10 Cross Territory Sales.

3.10.1 Each Party shall use Commercially Reasonable Efforts (consistent with any applicable Law) to obligate its sublicensees, distributors or wholesalers to not deliver or cause to be delivered Product outside such Party's Territory and to not sell any Product to a purchaser if in either case such sublicensees, distributors or wholesalers know, or have reason to believe, that such

purchaser intends to remove such Product from such Party's Territory for the purpose of sales or use by patients of Product in the other Party's Territory.

3.10.2 If either Party becomes aware that (i) a Product distributed and sold by a Party (the "**Distributing Party**"), its Affiliates, sublicensees, distributors or wholesalers is imported, distributed or sold in or to a country in the other Party's Territory ("**Cross-Territory Sales**"), and (ii) such Cross-Territory Sales (calculated by reference to the other Party's relevant average selling price(s), adjusted for different dosages) in such country in any calendar year reach or exceed [**] percent ([**]%) of the aggregate Net Sales (with such net sales by Akcea, its Affiliates or licensees determined in the same manner as Net Sales hereunder, *mutatis mutandis*) of the applicable Product in such country during the same period, then such Distributing Party shall promptly notify the other Party (the "**Cross-Territory Sales Notice**").

3.10.3 Within [**] after receipt or delivery, as the case may be, of such Cross-Territory Sales Notice, the Distributing Party shall prepare and submit to the other Party a written plan providing in reasonable detail the commercially reasonable steps and actions the Distributing Party, its Affiliates and its sublicensees, wholesalers and distributors shall take (consistent with any applicable Law) to prevent or limit the continued entry of Products into the other Party's Territory from the Distributing Party's Territory (the "**Cross-Territory Sales Report**") and present such report to the JSC for review and comment. From and after the JSC's adoption of such report, amended as the JSC may decide, the Distributing Party shall (a) use Commercially Reasonable Efforts (consistent with any applicable Laws) to implement the measures specified in such Cross-Territory Sales Report, (b) monitor and evaluate compliance with the requirements of the Cross-Territory Sales Report, and (c) assess, on a regular basis and in no event less often than [**], whether the conduct of the activities required by the Cross-Territory Sales Report have been successful in preventing or limiting the entry of Products from the Distributing Party's Territory into the other Party's Territory; *provided* that so long as the Distributing Party is in compliance with Sections 3.10.1 and 3.10.3(a)-(c), the failure of the measures specified in the applicable Cross-Territory Sales Report to actually prevent or limit the entry of Product from the Distributing Party's Territory into the other Party's Territory shall not be considered a material breach of this Agreement.

ARTICLE 4
MANUFACTURING

4.1 Supply Agreement. Within [**] after the Effective Date, the Parties shall negotiate in good faith a manufacturing and supply agreement (the "**Supply Agreement**") that sets forth mutually agreed terms and conditions under which Akcea and/or Ionis Pharmaceuticals, as applicable, will manufacture and supply, or cause to be manufactured and supplied by one or more Third Parties selected by Akcea, Drug Product for the Products to PTC, in quantities reasonably sufficient to support Commercialization of the Products by PTC and its Affiliates and Sublicensees in the PTC Territory through [**]. Akcea will sell to PTC, and PTC will purchase from Akcea, such Drug Product under the Supply Agreement in accordance with a mutually agreed forecast and supply schedule. Notwithstanding anything to the contrary set forth in this Section 4.1, PTC shall have the right, and Akcea shall in good faith support PTC, to enter into one or more supply agreement(s) for the supply of API and/or Drug Product for one (1) or more of the Products directly with Akcea's or its Affiliate's contract manufacturing organization(s) ("**CMO(s)**").

ARTICLE 5
MANAGEMENT OF THE COLLABORATION

5.1 Joint Steering Committee and Subcommittees.

5.1.1 The Parties hereby establish the Joint Steering Committee (the "**JSC**") to serve as the high-level oversight and decision-making body for the activities to be conducted by the Parties pursuant to this Agreement, as more fully described in this ARTICLE 5. The Parties anticipate that the JSC will not be involved in day-to-day implementation of the activities under this Agreement, but shall serve as the high-level oversight and decision-making body during the Term of this Agreement. The JSC may establish subcommittees as set forth in Section 5.2.

5.1.2 Responsibilities. The JSC shall perform the following functions, subject to the final decision-making authority of the respective Parties as set forth in Section 5.4:

(a) review the progress reports submitted by Akcea pursuant to Section 2.2 on the status of Development activities conducted by Akcea and Ionis Pharmaceuticals and the timing and likelihood of obtaining Regulatory Approval in any country within the PTC Territory;

(b) review and approve the Product Regulatory Strategy for each Product in the PTC Territory developed by the Parties pursuant to Section 2.4.2 and each annual update thereto;

(c) review the PTC Commercialization Plan submitted by PTC each Calendar Year pursuant to Section 3.2;

(d) review and approve the Product Trademark to be used in connection with the Commercialization of such Product in the PTC Territory, and develop any trademark usage guidelines relating to each such Product Trademark, it being understood that each party shall independently make the decisions set forth in Section 7;

(e) serve as a forum for discussions on market access, reimbursement and pricing strategy globally;

(f) review and approve global safety monitoring standards provided by Akcea; and

(g) review and approve the PTC Commercialization Targets for a Calendar Year as set forth in the PTC Commercialization Plan submitted by PTC to the JSC as set forth in Section 3.2.

For clarity, the JSC shall not have any authority beyond the specific matters set forth in this Section 5.1.2, and in particular shall not have any power to amend or modify the terms of this Agreement or waive a Party's compliance with this Agreement.

5.2 Formation and Dissolution of Subcommittee(s). The JSC may in its discretion, establish subcommittees from time to time to handle specific matters within the scope of the JSC's area of authority and responsibility (each, a "**Subcommittee**"), and no Subcommittee's authority and responsibility may be greater than that of the JSC itself. Each Subcommittee shall have such authority and responsibility as determined by the JSC from time to time, and decisions and recommendations of any Subcommittee shall be made in accordance with Section 5.4. The JSC shall determine when each Subcommittee it forms shall be dissolved.

5.2.1 Membership. Each of the JSC and each Subcommittee (each, a "**Committee**") shall be composed of an equal number of representatives appointed by each of Akcea and PTC. Each Committee shall be comprised of [**] representatives of each Party, or such other number as agreed upon by such Committee which may be less in number for any Subcommittee. Each individual appointed by a Party as a representative to a Committee shall be an employee of such Party, except that Akcea may appoint no more than [**]from Ionis Pharmaceuticals as one of its representatives to the JSC. Either Party may replace any or all of its Committee representatives at any time upon written notice to the other Party which notice may be given by e-mail sent to the other Party's co-chairperson of such Committee. Each Committee shall be co-chaired by one designated representative of each Party, which in the case of Akcea, may not be a representative from Ionis Pharmaceuticals. Any member of a Committee may designate a substitute to attend and perform the functions of that member at any meeting of such Committee, subject to Akcea's requirement to appoint no more than [**] of its representatives from Ionis Pharmaceuticals and subject to the other requirements set forth in this Section 5.2.1. Notwithstanding the foregoing, each Party shall ensure at all times during the existence of a Committee, its representatives on such Committee are appropriate in terms of seniority, experience, expertise and decision-making authority.

5.3 Meetings.

5.3.1 The co-chairpersons shall be responsible, with respect to their Committee for (a) calling meetings; (b) preparing and circulating an agenda in advance of each meeting; provided, that the co-chairpersons shall include any agenda items proposed by either Party on such agenda; (c) ensuring that all decision-making is carried out in accordance with the voting and dispute resolution mechanisms set forth in this Agreement; and (d) preparing and issuing minutes of each meeting within [**] (or such shorter time as is agreed by the relevant Committee) thereafter. The location of regularly scheduled meetings shall alternate between Akcea's offices located in Cambridge, Massachusetts, and PTC's offices located in Dublin, Ireland, unless otherwise agreed by such Committee. Such Committee may also determine that a meeting will instead be held telephonically, by video conference or by any other media. For the avoidance of doubt, each Party may designate the same individual as a representative on more than one Committee, except that Akcea may not appoint a representative from Ionis Pharmaceuticals to any Committee other

than the JSC. Each representative of a Party on a Committee shall be subject to confidentiality obligations no less stringent than those set forth in ARTICLE 11. Each Party will bear all expenses it incurs in regard to participating in all meetings of each Committee, including all travel and living expenses.

5.3.2 The JSC shall meet at least [**], and more or less frequently as the Parties mutually deem appropriate, on such dates and at such places and times as provided herein or as the Parties shall agree.

5.4 Decision-Making.

(a) Escalation to JSC. Except as otherwise provided herein, all decisions of each Committee shall be made by consensus, with all of a Party's voting members collectively having one (1) vote. Decisions of each Committee shall be made by unanimous vote. If a Committee other than the JSC is incapable of reaching unanimous agreement on a matter before it within [**], the matter shall be referred to the JSC for resolution. If the JSC is incapable of reaching unanimous agreement on a matter before it within [**], the matter shall be resolved in accordance with Section 5.4(b) (and, if applicable, Section 5.4(c)).

(b) Escalation to the Executive Officers. If the JSC cannot agree on a matter within [**] after it has met and attempted to reach such decision, then either Party may, by written notice to the other, have such issue referred to the Executive Officers for resolution. The Parties' respective Executive Officers shall meet within [**] after such matter is referred to them and shall negotiate in good faith to resolve the matter.

(c) Escalation to the Parties. If the Executive Officers are unable to resolve the matter within [**] after the matter is referred to them, then the issue shall be finally resolved as follows:

(i) PTC shall have final decision-making authority with respect to any disputes solely affecting [**], except for the determination as to whether (y) [**], or (z) [**];

(ii) Akcea shall have final decision-making authority with respect to whether [**];

(iii) while the JSC shall serve as the forum for the Parties for discussions on market access, reimbursement and pricing strategy globally, notwithstanding anything to the contrary set forth herein, each Party shall have sole authority with regard to setting pricing and reimbursement policies for each Product in their respective Territory but shall take into account the global impact of these decisions; and

(iv) with respect to any other dispute not specifically falling under Section 5.4(c)(i) – 5.4(c)(iii) above, neither Party shall have final decision-making authority with respect to such dispute.

provided, *however*, that (y) in no event shall any Committee or any Party alone have the power or authority to (1) amend this Agreement, (2) determine that a Party has fulfilled its obligations under Agreement or that the other Party has breached this Agreement, (3) make a decision that expressly requires the mutual agreement of the Parties or (4) require any Party to perform any act that such Party reasonably believes to be inconsistent with any Law. Any decision made by the Executive Officers in accordance with Section 5.4(b) or by a Party in accordance with this Section 5.4(c) shall be considered a decision made by the JSC.

5.5 Alliance Managers. Promptly after the Effective Date, each Party shall appoint an individual (who may not be a then-current member of the JSC or, in the case of Akcea, a representative of Ionis Pharmaceuticals) to act as alliance manager for such Party (each, an "**Alliance Manager**"). Each Alliance Manager shall thereafter be permitted to attend meetings of the JSC as a nonvoting observer, subject to the confidentiality provisions of ARTICLE 11. The Alliance Managers shall be the primary point of contact for the Parties regarding the activities contemplated by this Agreement. The Alliance Managers shall also be responsible for assisting the JSC in performing its oversight responsibilities. The name and contact information for each Party's Alliance Manager, as well as any replacement chosen by such Party, in its sole discretion, from time to time, shall be promptly provided to the other Party in accordance with Section 15.6.

5.6 Authority. In furtherance thereof, each Party will retain the rights, powers and discretion granted to it under this Agreement and no such rights, powers or discretion will be delegated to or vested in the JSC or any other Subcommittee unless such delegation or vesting of rights is expressly provided for in this Agreement or the Parties expressly so agree in writing.

ARTICLE 6
GRANT OF LICENSES

6.1 License Grant. Subject to the terms and conditions of this Agreement, Akcea grants to PTC, and PTC accepts:

6.1.1 an exclusive (even as to Akcea and its Affiliates, including Ionis Pharmaceuticals), royalty-bearing, non-transferable (except in accordance with Section 15.3), sublicensable (subject to Section 6.4) license under the Akcea Product-Specific IP to Exploit the Compounds and the Products in the PTC Territory (the "**Exclusive License**"); and

6.1.2 a non-exclusive, royalty-bearing, non-transferable (except in accordance with Section 15.3), sublicensable (subject to Section 6.4) license under the Akcea Core Technology IP and Akcea Manufacturing IP to (a) Exploit the Compounds

and the Products in the PTC Territory, and (b) Manufacture the Compounds and the Products in the Territory to the extent provided in the Supply Agreement and Section 4.1 (the "**Non-Exclusive License**").

Notwithstanding anything to the contrary set forth herein, until the date of payment in full of the Initial Fee by PTC, the license grants to PTC with respect to Compounds and Products containing volanesorsen may not be exercised by PTC, *provided that* (a) the obligations of the Parties under ARTICLE 7 shall remain in full force and effect; and (b) neither Akcea, Ionis Pharmaceuticals, nor any of their Affiliates shall otherwise encumber the Products, Compounds or the Akcea IP relating to volanesorsen.

6.2 In-License Agreements.

6.2.1 PTC acknowledges and agrees that the rights, licenses and sublicenses granted by Akcea to PTC in this Agreement are subject to the terms of the In-License Agreements, the scope of the licenses granted to Akcea or the applicable Affiliate thereunder and the rights granted to or retained by Ionis Pharmaceuticals, the Third Party counterparties, and any other Third Parties (each, an "**Inbound Licensor**") set forth therein. Akcea has, prior to the Effective Date, provided PTC with a true and complete copy of each Existing In-License Agreement.

6.2.2 If, after the Effective Date, Akcea or any of its Affiliates enters into a Future In-License Agreement with a Third Party pursuant to which Akcea (or, subject to Section 15.3, any of its Affiliates) obtains Control over a Third Party's Know-How or Patent Right that is necessary for the Exploitation of a Product in the PTC Territory, such Third Party's Know-How or Patent Rights shall be included in the license granted to PTC under Section 6.1.1 and considered Akcea IP hereunder if PTC agrees in writing to pay Akcea any and all costs arising under such Future In-License Agreement as they apply to such Product in the PTC Territory. Akcea shall provide PTC with a true and complete copy of each of any Future In-License Agreement promptly after such Future In-License Agreement has been fully executed and delivered by the parties thereto.

6.2.3 PTC covenants to Akcea to comply with, and to cause its Affiliates and Sublicensees to comply with, the terms and conditions of the In-License Agreements. To the extent there is a conflict between any of the terms of any In-License Agreement and the rights granted to PTC hereunder (including with respect to any sublicensing rights, diligence obligations, Prosecution and Maintenance, enforcement and defense rights), the terms of such In-License Agreement shall control with respect to the Know-How and Patent Rights owned or controlled by, or subject to the rights of, such Inbound Licensor under such In-License Agreement.

6.2.4 The Parties acknowledge that the terms of any In-License Agreement may be subject to interpretation. The Parties shall cooperate with each other in good faith to support each other in complying with each other's obligations under each In-License Agreement. Without limitation to the foregoing, the Parties shall, from time to time, upon the reasonable request of either Party, discuss the terms of any applicable In-License Agreement and agree upon, to the extent reasonably possible, a consistent interpretation of the terms of such In-License Agreement in order to, as fully as possible, allow each Party to comply with the terms of such In-License Agreement. If a Party believes an interpretation is or may be incorrect, such Party shall share such conclusion or information with the other Party, subject to any confidentiality obligations owed by Akcea to the relevant Inbound Licensor, and the Parties shall discuss such conclusion or information.

6.2.5 Without limiting the foregoing, PTC shall prepare and deliver to Akcea any additional reports required under the applicable In-License Agreements of Akcea, in each case (a) sufficiently in advance to reasonably enable Akcea to comply with its obligations under the applicable In-License Agreements, and (b) to the extent that Akcea provides reasonable notice to PTC regarding any such report and the requirements thereto.

6.3 Effect of Termination on Sublicenses. If any In-License Agreement terminates for any reason PTC will, from the effective date of such termination, automatically become a direct licensee of the Inbound Licensor with respect to the rights sublicensed to PTC by Akcea; *so long* as (i) PTC is not in material breach of this Agreement, (ii) PTC agrees in writing to comply with all of the terms of this Agreement to the extent applicable to the rights originally sublicensed to it by Akcea, and (iii) PTC agrees to pay directly to the applicable Inbound Licensor PTC's payment under this Agreement to the extent applicable to the rights sublicensed to it by Akcea. Akcea agrees that it will confirm clause (i) of the foregoing in writing at the request and for the benefit of PTC. Without limiting the generality of the foregoing and in furtherance thereof, contemporaneous with the execution of this Agreement, as of the Effective Date, Ionis Pharmaceuticals has executed and delivered to PTC a written acknowledgement and consent in the form mutually agreed by the Parties.

6.4 PTC's Sublicensing Rights. PTC may grant and authorize sublicenses under the rights granted to it under Section 6.1 to any of its Affiliates and to any Third Parties that are Permitted Sublicensees (each such Affiliate or Permitted Sublicensees, a "**Sublicensee**"). PTC shall provide Akcea with a fully-executed copy of any agreement (redacted as necessary to protect confidential or commercially sensitive information that is not necessary for Akcea to determine PTC's compliance with this Agreement or for Akcea to comply with the In-License Agreements) reflecting any such sublicense promptly (but no later than [**]) after the execution thereof (a "**Sublicense**"). PTC assumes full responsibility, and shall remain primarily liable, for causing the performance of all obligations of each of its Sublicensees, and will itself pay and account to Akcea for all payments due under this Agreement by reason of operation of any such Sublicense. Each Sublicense must be consistent with, and require its Sublicensee to meet, all applicable obligations and requirements of the In-License Agreements.

6.5 Licenses to Akcea. Subject to the terms and conditions of this Agreement, PTC hereby grants to Akcea, and Akcea accepts, a non-exclusive, royalty-free, non-transferable (except in accordance with Section 15.3), sublicensable (only to Permitted Sublicensees) license under the PTC Product-Specific IP to Exploit any products anywhere in the world, except that such license shall not apply to the Exploitation of any Products in the PTC Territory being Exploited by PTC or its Affiliates or Sublicensees. Akcea assumes full responsibility, and shall remain primarily liable, for causing the performance of all obligations of each of its Sublicensees. Each Sublicense must be consistent with, and require its Sublicensee to meet, all applicable obligations and requirements of the In-License Agreements.

6.6 No Other Rights. Except as otherwise expressly provided in this Agreement, under no circumstances shall a Party, as a result of this Agreement, obtain any ownership interest, license right or other right in any Know-How, Patent Rights or other intellectual property rights of the other Party or any of its Affiliates, including items owned, controlled, developed or acquired by the other Party or any of its Affiliates, or provided by the other Party to the first Party at any time pursuant to this Agreement.

6.7 Section 365(n) of the Bankruptcy Code. All rights and licenses granted under or pursuant to this Agreement by a Party to the other, including those set forth in Section 6.1 and 6.4, are and shall otherwise be deemed to be, for purposes of Section 365(n) of the U.S. Bankruptcy

Code or any foreign counterpart thereto, licenses of right to "intellectual property" as defined under Section 101 of the U.S. Bankruptcy Code or any foreign counterpart thereto. The Parties agree that the Parties shall retain and may fully exercise all of their rights and elections under the U.S. Bankruptcy Code and any foreign counterpart thereto. All payments to be made by PTC under this Agreement or any ancillary agreement (such as any supply agreement), including the Initial Fee, milestone payments and royalties, shall be considered "royalties" for purposes of Section 365(n) of the U.S. Bankruptcy Code.

ARTICLE 7
EXCLUSIVITY; RIGHT OF FIRST NEGOTIATION

7.1 Exclusivity.

7.1.1 Exclusivity Covenants. Except in the performance of its obligations or exercise of its rights under this Agreement and except as set forth in Section 7.1.2 or Section 7.2, subject to the terms of this Agreement, neither Party nor any of its respective Affiliates shall, either alone or with or for any Third Party, work independently or for or with any Third Party (including the grant of any license to any Third Party) with respect to the Commercialization in the PTC Territory of an oligonucleotide that is designed to bind to the RNA that encodes TTR, from the Effective Date until, on a country-by-country basis in the PTC Territory, [**].

7.1.2 Limitations and Exceptions to Akcea's Exclusivity Covenants. Notwithstanding anything to the contrary in this Agreement, Akcea's practice of the following will not violate Section 7.1.1:

(a) Any activities pursuant to the Prior Agreements as in effect on the Effective Date;

(b) The granting of, or performance of obligations under, Permitted Licenses;

(c) The exercise of Akcea's rights under Section 7.2; and

(d) Subject to Section 7.2, the Commercialization of AKCEA-TTR-L_{Rx} in the PTC Territory.

7.2 Right of First Negotiation; Inotersen Buy-Out.

7.2.1 During the Term and subject to the terms of this Agreement, Akcea hereby grants to PTC a right of first negotiation (the "**ROFN Right**") to Commercialize AKCEA-TTR-L_{Rx} on an exclusive basis in the PTC Territory (the "**Proposed Transaction**"). Akcea and Ionis shall not enter into any agreement or grant any license to AKCEA-TTR-L_{Rx} inconsistent with the provisions of this Section 7.2. As soon as reasonably practicable following completion of the [**], Akcea shall prepare and provide to PTC a data package containing at a minimum [**] (the "**Evaluation Package**") and shall make a presentation to the JSC that covers at a minimum [**] (the "**JSC Evaluation Presentation**"). Both Parties shall require appropriate internal and external experts reasonably necessary to present and evaluate the Evaluation Package and JSC Evaluation Presentation to attend such JSC meeting, and such JSC meeting shall allow sufficient time for the experts to engage in a robust question and answer session. Within [**] after the later of Akcea's delivery of the Evaluation Package and JSC Evaluation Presentation, PTC shall indicate to Akcea in writing whether it wishes to enter into the Proposed Transaction and, if PTC indicates that it wishes to enter into the Proposed Transaction, the Parties shall negotiate in good faith mutually agreeable terms pursuant to which the Parties would enter into such Proposed Transaction, including agreement on an upfront fee and regulatory milestone payments commensurate with the value of AKCEA-TTR-L_{Rx} at such time, *provided that* the royalty rate for AKCEA-TTR-L_{Rx} shall be the same as the royalty rate and royalty term for inotersen under Section 9.3. If either (a) PTC indicates it does not wish to enter into such Proposed Transaction, (b) PTC fails to indicate its interest within such [**] period or (c) PTC indicates it wishes to enter into such Proposed Transaction but the Parties fail to execute a definitive agreement with respect to such Proposed Transaction within [**] after Akcea's receipt of PTC's indication of interest, then the ROFN Right shall expire (the "**Expiration of the ROFN Right**").

7.2.2 Within [**] after the Expiration of the ROFN Right, Akcea shall notify PTC whether Akcea, Ionis Pharmaceuticals and/or one of their respective Affiliates plans (a) [**], or (b) [**]. If Akcea fails to notify PTC within such [**] period, then Akcea shall automatically be deemed to have exercised the Inotersen Buy-Out Option, in which case the procedures set forth in Sections 7.2.3(a) – (d) shall apply.

7.2.3 If Akcea either (i) gives PTC notice pursuant to Section 7.2.2(a) that [**], or (ii) fails to provide any notice to PTC within the [**] period provided in Section 7.2.2, then PTC may by written notice to Akcea within [**] thereafter exercise its option for Akcea to purchase back PTC's rights to inotersen (the "**Inotersen Buy-Out Option**"), in which case the following procedure shall apply:

(a) the Parties shall meet to discuss in good faith a written amendment to this Agreement pursuant to which Akcea would make a one-time payment to PTC based on the [**], taking into account, among other relevant factors, [**] (the "**Inotersen FMV**") in exchange for the [**] and the [**] (the "**Inotersen Buy-Out**").

(b) If the Parties cannot agree upon and execute such an amendment within [**] after Akcea has exercised the Inotersen Buy-Out Option, then within [**] after the expiration of such [**] period, each Party shall provide the other Party in writing with such Party's last best offer with respect to the Inotersen FMV and the terms and conditions of the Inotersen Buy-Out in writing (each, a "**Final Offer**). If the Parties cannot promptly choose one Party's Final Offer to apply to the Inotersen Buy-Out, then either Party shall at any time have the right, upon written notice to the other Party (a "**Valuation Notice**"), to engage one (1) independent, impartial and neutral Third Party valuation expert (a "**Valuation Expert**") to determine which Party's Final Offer shall apply to the Inotersen Buy-Out. The Valuation Expert shall be mutually agreed to by the Parties; *provided that* if the Parties cannot agree on one (1) Valuation Expert within [**] after a Party provides the other party with a Valuation Notice, then each Party shall select one (1) Third Party Valuation Expert and those two (2) Third Party Valuation Experts will select the one (1) Valuation Expert within [**] thereafter, which one (1) Valuation Expert selected shall determine which Party's Final Offer shall apply to the Inotersen Buy-Out; *provided further* that any selected Valuation Expert shall not be a current or former employee, officer, director, consultant or subcontractor of either Party or any of its Affiliates. The Parties shall use their best efforts to cooperate in good faith and cause the Valuation Expert to be retained as soon as possible after the selection of such Valuation Expert after a Party provides the other Party with a Valuation Notice.

(c) Each Party shall submit to the Valuation Expert and the other Party (i) the Final Offer such Party provided to the other Party pursuant to clause (b) above and such information concerning the Inotersen FMV as such Party may deem appropriate, within [**] after the retention of the Valuation Expert, and (ii) such other information as may be requested by the Valuation Expert within [**] after such request. Any such information provided to the Valuation Expert by a Party shall be simultaneously provided to the other Party. The Valuation Expert shall determine the Inotersen FMV and the terms and conditions of the Inotersen Buy-Out within [**] after its receipt of the Final Offer by selecting one (1) or the other of the two (2) Final Offers submitted by the Parties (such selected Final Offer, the "**Selected Final Offer**"), which determination shall take into account, among other relevant factors, [**]. The Valuation Expert's determination will be final and shall serve as the only terms and conditions for the Inotersen Buy-Out. The Valuation Expert shall promptly notify the Parties of such Selected Final Offer in writing. Upon such notification, unless Akcea provides written notice to PTC under Section 7.2.3(d) below, the Parties shall in good faith promptly perform the terms and conditions of the Selected Final Offer.

(d) Notwithstanding the foregoing, if the Valuation Expert selects PTC's Final Offer as the Selected Final Offer, then within [**] after the date the Valuation Expert notifies the Parties of such Selected Final Offer, Akcea may provide written notice to PTC that Akcea does not desire to consummate the Inotersen Buy-Out under the terms and conditions of the Selected Final Offer. If Akcea provides such a written notice to PTC within such [**] period, then (i) Akcea will have no obligation to consummate the Inotersen Buy-Out under the terms and conditions of the Selected Final Offer, and (ii) unless otherwise mutually agreed to by the Parties in writing, neither Akcea, Ionis Pharmaceuticals nor any of their respective Affiliates will sell AKCEA-TTR-L_{Rx} in the PTC Territory during the Royalty Term for inotersen.

7.2.4 If Akcea, Ionis Pharmaceuticals and/or one of their respective Affiliates (as the case may be, an "**Akcea Proposed Transaction Entity**") elects to enter into a Proposed Transaction with a Third Party, then such Akcea Proposed Transaction Entity will have the right, but not the obligation, to enter into such a Proposed Transaction, *provided that* the terms of such a Proposed Transaction entered into by such Akcea Proposed Transaction Entity within [**] after the Expiration of the ROFN Right must be [**]. Akcea shall provide an unredacted copy of the fully-executed agreement that the Akcea Proposed Transaction Entity enters into with such Third Party for the Proposed Transaction, so that PTC may verify that Akcea has complied with this Section 7.2.4. After the [**] anniversary of the Expiration of the ROFN Right, an Akcea Proposed Transaction Entity will have the right, but not the obligation, to enter into a Proposed Transaction on any terms (including on terms that are [**]), in Akcea's sole discretion.

ARTICLE 8
GENERAL PROVISIONS RELATING TO COLLABORATION

8.1 Compliance. All Development, Manufacturing and Commercialization activities conducted by a Party under this Agreement shall be conducted in compliance with applicable Laws, including cGMP, cGLP and cGCP.

8.2 Subcontracting. Each Party shall have the right to engage Affiliates or Third Party subcontractors to perform certain of its obligations under this Agreement at its sole discretion. Any Affiliate or Third Party subcontractor to be engaged by a Party to perform a Party's obligations set forth in this Agreement shall meet the qualifications typically required by such Party for the performance of work similar in scope and complexity to the subcontracted activity; provided that, any Party engaging an Affiliate or Third Party subcontractor hereunder shall remain principally responsible and obligated for such activities. In addition, each Party engaging a subcontractor with respect to its obligations shall in all cases use commercially reasonable efforts to retain or obtain exclusive Control of any and all Know-How, Patent Rights or other intellectual property created by such subcontractor directly related to such subcontracted activity.

8.3 Records and Audits. Each Party shall, and shall require its Affiliates and subcontractors to, maintain materially complete, current and accurate hard and electronic (as applicable) copies of records of all work conducted pursuant to its Development, Manufacturing and Commercialization activities under this Agreement, and all results, data, developments and Know-How made in conducting such activities. Such records shall accurately reflect all such work done and results achieved in sufficient detail and in good scientific manner appropriate for applicable patent and regulatory purposes.

ARTICLE 9
INITIAL FEE; MILESTONES AND ROYALTIES; PAYMENTS

9.1 Initial Fee. In partial consideration for the rights and licenses granted to PTC hereunder, PTC shall pay to Akcea a total amount of eighteen million U.S. Dollars ($18,000,000) in the following manner (together, the "**Initial Fee**"):

9.1.1 A non-refundable, non-creditable, irrevocable payment of twelve million U.S. Dollars ($12,000,000) within ten (10) Business Days after the Effective Date.

9.1.2 A non-refundable, non-creditable, irrevocable payment of six million U.S. Dollars ($6,000,000) to be paid within thirty (30) days of receipt of Regulatory Approval from the FDA or the EMA of volanesorsen.

9.2 Regulatory Milestone Payments. In further consideration for the rights and licenses granted to PTC hereunder, on a Product-by-Product basis, PTC shall pay Akcea a non-refundable, non-creditable, irrevocable milestone payment of four million U.S. Dollars ($4,000,000) upon the first achievement for each such Product of receipt of Regulatory Approval from ANVISA (each, a "**Milestone Payment**"). PTC shall pay each Milestone Payment within thirty (30) days after receipt by PTC of formal written notice from ANVISA has granted Regulatory Approval for a Product for Brazil. For purposes of clarity, the maximum aggregate payments under this Section 9.2 shall be eight million U.S. dollars ($8,000,000).

9.3 Royalties. In further consideration of the licenses and other rights granted to PTC, on a country-by-country and Product-by-Product basis, during the Royalty Term, PTC shall pay to Akcea royalties in respect of Net Sales of such Product by PTC, its Affiliates and Sublicensees in the PTC Territory at a royalty rate of [**] percent ([**]%) of Net Sales (the "**Royalty Rate**").

9.4 Royalty Period. PTC's obligation to pay Akcea the royalties under Section 9.3 above with respect to a Product will continue on a country-by-country and Product-by-Product basis from the Royalty Trigger Date for such Product and will terminate upon the later of: (a) the date of expiration, invalidation or abandonment of the last Valid Claim within the Akcea Patent Rights Covering such Product in the country in which such Product is made, used or sold; (b) ten (10) years from the First Commercial Sale of such Product in Brazil; and (c) expiration of Regulatory Exclusivity for such Product in such country (the applicable "**Royalty Term**").

9.5 Royalty Adjustments – Comparable Third Party Product Competition; Compulsory Licensing. If, on a Product-by-Product, country-by-country and Calendar Quarter-by-Calendar Quarter basis, (a) Comparable Third Party Product Competition is present with respect to such Product in a country in the PTC Territory during such Calendar Quarter; or (b) a court or other Governmental Authority of competent jurisdiction requires PTC or any of its Affiliates or Sublicensees to grant a compulsory license to a Third Party permitting such Third Party to Commercialize such Product in such country (such Product when sold by such Third Party under subsection (a) or (b), a "**Compulsory Third Party Product**"), and such Compulsory Third Party Product(s) has a market share of [**] percent ([**]%) or more of the aggregate market in such country of the applicable Product (such market share percentage, the "**Market Share Loss Percentage**"), then, subject to Section 9.6, the royalty rate under Section 9.3 used to calculate the payment of royalties payable with respect to Net Sales of such Product pursuant to Section 9.3 in such country during such Calendar Quarter shall be reduced by an amount equal to the actual Market Share Loss Percentage. For example, if the Market Share Loss Percentage in a given country in the PTC Territory is [**]%, then the royalty rate under Section 9.3 used to calculate the payment of royalties payable with respect to Net Sales of such Product pursuant to Section 9.3 in such country during such Calendar Quarter shall be reduced by [**]% to a royalty rate of [**]% [**].

9.6 Limits on Deductions. In no event shall the cumulative effect of the adjustment set forth in Section 9.5 (in the order in which the event triggering such reduction occurs) reduce the royalties payable to Akcea pursuant to Section 9.3 to less than [**] percent ([**]%) of the amounts that would otherwise have been payable with respect to the applicable Product in the applicable country in the applicable Calendar Quarter, as determined pursuant to Section 9.3. Credits for adjustments pursuant to this Section 9.6 not exhausted in any Calendar Quarter may be carried into future Calendar Quarters, subject to the preceding sentence.

9.7 Reports; Payment of Royalty. During the Term, following the First Commercial Sale of any Product in any country in the Territory, PTC shall furnish to Akcea a written report within [**] after the end of each of the first three (3) Calendar Quarters during a Calendar Year and [**] of the final Calendar Quarter of such Calendar Year showing, on a Product-by-Product and country-by-country basis, the Net Sales of each Product in each country of the PTC Territory and the royalties payable under this Agreement. Royalties with respect to Net Sales of Products shall be due and payable on the date such royalty report is due. In addition, beginning with the Calendar Quarter in which the First Commercial Sale for a Product is made and for each Calendar Quarter thereafter, within [**] following the end of each such Calendar Quarter, PTC will provide Akcea a preliminary non-binding report estimating the total Net Sales of, and royalties payable to Akcea for Products projected for such Calendar Quarter.

9.8 Accounting.

9.8.1 PTC agrees to keep, and to require its Affiliates and Sublicensees to keep, full, clear and accurate records for a minimum period of [**] years after the relevant payment is owed pursuant to this Agreement, setting forth the sales and other

disposition of Products sold or otherwise disposed of, in sufficient detail to enable royalties and compensation payable to Akcea hereunder to be determined.

9.8.2 PTC further agrees, upon not less than [**] prior written notice, to permit, and to require its Affiliates and Sublicensees to permit, such books and records relating to such Products to be examined by an independent accounting firm selected by Akcea and reasonably acceptable to PTC for the purpose of verifying reports provided (or required to be provided) by PTC under this ARTICLE 9. Such audit shall not be performed more frequently than [**] period, and shall be conducted under appropriate confidentiality provisions, for the sole purpose of verifying the accuracy and completeness of all financial, accounting and numerical information and calculations provided under this Agreement. The independent accounting firm shall only share the results of the audit, not the underlying records, with Akcea.

9.8.3 Such examination is to be made at the expense of Akcea, except if the results of the audit reveal an underpayment of royalties, milestones or other payments to Akcea under this Agreement, of [**] percent ([**]%) or more, then the reasonable fees and expenses for such examination shall be paid by PTC.

9.9 Methods of Payments. All payments due from one Party to the other Party under this Agreement shall be paid in Dollars by wire transfer to a bank in the United States designated in writing by the payee.

9.10 Taxes.

9.10.1 Subject to Section 9.10.2, each Party shall be solely responsible for the payment of all taxes imposed on its share of income arising directly or indirectly from the activities of the Parties under this Agreement.

9.10.2 In the event that PTC is required to withhold any tax to be paid to, or held for the benefit of, the tax or revenue authorities in any country in the Territory regarding any payment to Akcea, such amount shall be deducted from the payment to be made by PTC and paid over to the relevant authorities. PTC shall promptly notify Akcea of such requirement and shall take reasonable and lawful actions requested by Akcea to avoid or minimize any such withholding. PTC shall promptly furnish Akcea with copies of any tax receipts or other documentation evidencing the fact and amount of such withholding. Each Party shall cooperate with the other Party in seeking reductions in, or exemptions from, any such withholding under any applicable tax treaty. Akcea shall use commercially reasonable efforts to provide documentation in support of any available reduction in, or exemption from, any such withholding.

9.10.3 The provisions of this Section 9.10 are to be read in conjunction with the provisions of Section 15.3 below.

9.11 Currency Exchange. Notwithstanding anything to the contrary in the Agreement, the Parties agree that PTC may use any generally accepted exchange rate methodology that PTC uses for all or substantially all of its global operations for the purposes of any currency conversions required in connection with the calculation of royalty payments to Akcea pursuant to the Agreement. Akcea acknowledges that PTC currently uses European Central Bank rates applied on a monthly basis and agrees that this methodology is acceptable for purposes the calculation of royalty payments to Akcea pursuant to the Agreement.

ARTICLE 10
INTELLECTUAL PROPERTY RIGHTS

10.1 Ownership of Inventions; Disclosure.

10.1.1 Existing IP. Nothing in this Agreement shall affect Akcea's ownership of the Akcea IP existing as of the Effective Date or PTC's ownership of PTC IP existing as of the Effective Date, which in each case shall remain owned by the Party having such rights.

10.1.2 Ownership. Except as set forth in Section 10.1.3, (a) title to all Know-How discovered, developed, invented or created solely by employees or agents of Akcea in the course of activities conducted pursuant to this Agreement and any Patent Rights that claim or cover such Know-How shall be owned by Akcea (each, an "**Akcea Invention**"); (b) title to all Know-How discovered, developed, invented or created solely by employees or agents of PTC in the course of activities conducted pursuant to this Agreement and any Patent Rights that claim or cover such Know-How shall be owned by PTC (each, a "**PTC Invention**"); and (c) title to all Know-How discovered, developed, invented or created jointly by employees or agents of PTC and Akcea in the course of activities conducted pursuant to this Agreement and any Patent Rights that claim or cover such Know-How shall be owned jointly by PTC and Akcea (each, a "**Joint Invention**"). Inventorship of inventions made pursuant to this Agreement shall be determined in accordance with the patent laws of the United States. Except as otherwise expressly provided in this Agreement, each Party may (subject to the exclusivity provisions of this Agreement and Section 6.5) practice, grant licenses under, and transfer (subject to the terms and conditions of this Agreement and Section 6.5) any Joint Invention, neither Party shall have any obligation to account to the other for profits, or to obtain any approval of the other Party to license or exploit any Joint Invention, by reason of joint ownership thereof, and each Party hereby waives any right it may have under the laws of any jurisdiction to require any such consent or accounting.

10.1.3 Exceptions. Notwithstanding Section 10.1.2 and anything to the contrary set forth in this Agreement, Akcea shall exclusively own any Akcea Invention, PTC Invention or Joint Invention that would constitute an Akcea Core Technology Patent Right or Akcea Core Technology Know-How hereunder (regardless of inventorship by Akcea or PTC) (the "**Akcea-Owned Categories**"). PTC, on behalf of itself and its Affiliates, hereby assigns, and to the extent such present assignment is not possible, agrees to assign, to Akcea all right, title and interest in and to such PTC Inventions and Joint Inventions that fall within the Akcea-Owned Categories, and all intellectual property rights therein, which such PTC Inventions or Joint Inventions shall thereafter be deemed to be "*Akcea Core Technology Patent Rights*" or "*Akcea Core Technology Know-How*" for purposes of this Agreement.

10.2 Patent Prosecution.

10.2.1 Akcea Patent Rights.

(a) Akcea shall be responsible, at its sole cost and expense, and shall have the exclusive right, but not the obligation, for Prosecuting and Maintaining the Akcea Core Technology Patent Rights, the Akcea Manufacturing Patent Rights and the Akcea Product-Specific Patent Rights. In addition, Akcea shall be responsible, and shall have the exclusive right, but not the obligation, for conducting any opposition, reexamination request, nullity action, interference, or other attack upon the validity, title or enforceability of the Akcea Core Technology Patent Rights, the Akcea Manufacturing Patent Rights and the Akcea Product-Specific Patent Rights (each, a "**Defense Proceeding**") in the Akcea Territory and the PTC Territory. The cost of any such Defense Proceeding of the Akcea Product-Specific Patent Rights in the PTC Territory will be shared equally by Akcea and PTC.

(b) With respect to the PTC Territory, Akcea shall (i) provide PTC with copies of the text of the applications for any Akcea Product-Specific Patent Right Covering a Product as soon as practicable but at least [**] before filing, except for urgent filings, in which case Akcea shall provide copies as soon as practicable before, simultaneously with or immediately after filing; (ii) provide PTC with a copy of each submission made to and material document received from a patent authority, court or other tribunal regarding any such Akcea Product-Specific Patent Right reasonably promptly after making such filing or receiving such material document, including a copy of each application as filed together with notice of its filing date and application number; (iii) keep PTC advised of the status of all material communications, actual and prospective filings or submissions regarding any such Akcea Product-Specific Patent Right and, as soon as practicable except for urgent filings and submissions, give PTC copies of any such material communications, filings and submissions proposed to be sent to any patent authority or judicial body; and (iv) consider in good faith and reasonably incorporate PTC's comments on the material communications, filings and submissions for any such Akcea Product-Specific Patent Right.

(c) Akcea shall notify PTC as to any decision to abandon, to cease Prosecution and Maintenance of, or not to continue to pay the expenses of Prosecution and Maintenance of, any such Akcea Product-Specific Patent Right Covering a Product in any country in the PTC Territory in which it was filed. Akcea will provide such notice as soon as practicable prior to any filing or payment due date, or any other due date that requires action, in connection with such Akcea Product-Specific Patent Right. Thereafter, PTC may, upon written notice to Akcea, in Akcea's name and at PTC's sole cost and expense, control the Prosecution and Maintenance of such Akcea Product-Specific Patent Right in the PTC Territory.

10.2.2 PTC Patent Rights. PTC shall be responsible, at its sole cost and expense, and shall have the exclusive right, but not the obligation, in the PTC Territory, (a) for Prosecuting and Maintaining the PTC Product-Specific Patent Rights, and (b) for conducting Defense Proceedings relating thereto.

10.2.3 Cooperation. Each Party shall reasonably cooperate with and assist the other Party in connection with the activities of such Party under this Section 10.2 upon the reasonable request of the other Party, including by making scientists and scientific records reasonably available and the execution of all such documents and instruments and the performance of such acts as may be reasonably necessary in order to permit the other Party to continue any Prosecution or Maintenance of such Patent Rights.

10.3 Enforcement and Defense.

10.3.1 Notice. If any Party learns of an infringement or threatened infringement by a Third Party with respect to any Akcea Patent Right or PTC Patent Right, including actual or alleged infringement under 35 USC §271(e)(2) or any foreign equivalent that is or would be competitive with a Compound or Product ("**Competitive Infringement**"), such Party shall promptly notify the other Party and shall provide such other Party with available evidence of such Competitive Infringement.

10.3.2 Actions.

(a) If any Akcea Product-Specific Patent Right Covering a Product is infringed by a Third Party in any country in the PTC Territory, then Akcea shall have the first right, but not the obligation, to institute, prosecute, and control any action or proceeding with respect to such infringement of such Patent Right, by counsel of its own choice. If in any such proceeding brought by Akcea, PTC is required to join for standing purposes or in order for Akcea to commence or continue any such proceeding, then PTC shall join such proceeding, at Akcea's expense, and shall be represented in such proceeding by counsel of PTC's choice at Akcea's expense.

(b) If Akcea does not bring an infringement action pursuant to Section 10.3.2(a) within [**] after receipt of notice of the existence of an infringement (or in cases where there is a relevant statutory period during which an infringement action must be commenced or in which any material rights may be lost that would expire prior to the expiration of such [**] period, [**] prior to the expiration of such relevant statutory period), Akcea and PTC shall meet and discuss Akcea's reasons for not initiating a lawsuit or otherwise making or prosecuting a claim. If after having given due consideration to Akcea's reasons, PTC desires to initiate a lawsuit or otherwise make or prosecute a claim of infringement, PTC shall so notify Akcea and PTC may thereafter institute, prosecute, and control such action at its sole cost and expense. If in any such proceeding Akcea is required to join for standing purposes or in order for PTC (or an Inbound Licensor) to commence or continue any such proceeding, then Akcea shall join such proceeding, at PTC's expense, and shall be represented in such proceeding by counsel of Akcea's choice at PTC's expense.

(c) Any exercise by PTC of the right to bring an infringement action shall be subject to and consistent with the terms of all applicable In-License Agreements; *provided that*, if, under the terms of an applicable In-License Agreement, Akcea has an applicable enforcement right that it cannot delegate to PTC then, at PTC's request and expense, Akcea shall use commercially reasonable efforts to exercise such rights in such infringement action as directed by PTC.

(d) The Party initiating the suit shall have the sole and exclusive right to elect counsel for any suit initiated by it pursuant to this ARTICLE 10; *provided that*, with respect to an Akcea Product-Specific Patent Right Covering a Product, such counsel is reasonably acceptable to the other Party.

(e) Each Party agrees to cooperate fully in any action under this Section 10.3.2 that is controlled by the other Party, including executing legal papers and cooperating in the prosecution as may be reasonably requested by the controlling Party, all at the controlling Party's expense.

(f) PTC shall have the sole right, but not the obligation, to institute, prosecute and control any action or proceeding with respect to any infringement of PTC Patent Rights.

(g) Unless otherwise agreed by the Parties in writing, the amount of any recovery from a proceeding brought under this Section 10.3.2 shall first be applied to the out-of-pocket costs of such action by the Party prosecuting the applicable action, and any remaining recovery amount shall be allocated first to the Inbound Licensor pursuant to the applicable In-License Agreement, if applicable, and then, of the remaining amount, (i) any recovery for a proceeding brought with respect to an Akcea Product-Specific Patent Right Covering a Product shall be shared equally by the Parties, (ii) any recovery for a proceeding brought with respect to an Akcea Patent Right other than an Akcea Product-Specific Patent Right Covering a Product shall be retained by Akcea, (iii) any recovery for a proceeding brought with respect to a PTC Product-Specific Patent Right shall be shared by the Parties such that PTC will receive [**] percent ([**]%) of any such recovery and Akcea will receive [**] percent ([**]%) of any such recovery, and (iv) any recovery for a proceeding brought with respect to a PTC Patent Right other than a PTC Product-Specific Patent Right shall be retained by PTC. If, in connection with a proceeding brought under this Section 10.3.2 with respect to an Akcea Product-Specific Patent Right Covering a Product, an Inbound Licensor is entitled to a portion of any recovery that is greater than the portion of the recovery payable, after costs, to Akcea, the Parties will meet and agree in good faith on an alternative sharing of such recovery to that set forth in the immediately preceding sentence that takes into account the amounts payable to the applicable Inbound Licensor and results in an equitable allocation of the remaining amounts to PTC and Akcea after payment of such amounts to the applicable Inbound Licensor.

10.3.3 Defense. With respect to any defense or declaratory judgment actions relating to or other attack upon valid title or enforcement of an Akcea Patent Right or PTC Patent Right, including any Defense Proceeding but excluding any Prosecution or Maintenance and any such action or attack is in connection with any counterclaim brought in actions subject to Section 10.3.2, the Party with responsibility for the Prosecution and Maintenance of such Patent Right shall have the first right, but not the obligation, to assume the defense thereof at its sole cost and expense. With respect to any Defense Proceeding relating to an Akcea Product-Specific Patent Right Covering a Product, (a) if Akcea defends such Patent Right, PTC shall have the right, at its sole cost and expense, to join any such defense with counsel of its choice, and (b) if Akcea declines to assume the defense of any such Patent Right, then PTC shall have the right, but not the obligation, to assume the defense thereof at its sole cost and expense. Each Party agrees to render such reasonable assistance as the defending Party may request, at the defending Party's expense, with respect to actions brought pursuant to Section 10.3.2.

10.4 Infringement Claimed by Third Parties.

10.4.1 If a Third Party commences, or threatens to commence, any proceeding against a Party alleging infringement of such Third Party's intellectual property by the Exploitation by a Party, its Affiliates, subcontractors or sublicensees of any Compound or Product, the Party against whom such proceeding is threatened or commenced shall give prompt notice to the other Party.

10.4.2 Unless the Party against whom such proceeding is filed seeks indemnification for a claim covered pursuant to ARTICLE 13, such Party shall control the defense and settlement of any such proceeding at its own cost.

10.5 Marking. PTC and its Affiliates and Sublicensees shall mark each Product in such a manner to conform with the patent laws and practice of any country in which such Product is Manufactured or sold or to which such Product is shipped to ensure maximum enforceability of Patent Rights in such country.

ARTICLE 11
CONFIDENTIALITY

11.1 Confidentiality; Exceptions. Except to the extent expressly authorized by this Agreement or otherwise agreed in writing, the Parties agree that the receiving Party (the "**Receiving Party**") shall keep confidential and shall not publish or otherwise disclose or use for any purpose other than as provided for in this Agreement any Know-How or other confidential and proprietary information and materials, patentable or otherwise, in any form (written, oral, photographic, electronic, magnetic, or otherwise) that is disclosed to it by the other Party (the "**Disclosing Party**"), including trade secrets, Know-How, inventions or discoveries, proprietary information, formulae, processes, techniques and information relating to the Disclosing Party's past, present or future marketing, financial, or Exploitation activities of any product or potential product or useful technology of the Disclosing Party or the pricing thereof (collectively, "**Confidential Information**"), except to the extent that it can be established by the Receiving Party that such Confidential Information:

11.1.1 was in the lawful knowledge and possession of the Receiving Party prior to the time it was first disclosed to the Receiving Party by the Disclosing Party, or was otherwise developed independently by the Receiving Party without reference to any of the Disclosing Party's Confidential Information, as evidenced by written records kept in the ordinary course of business, or other documentary proof of actual use by the Receiving Party;

11.1.2 was generally available to the public or otherwise part of the public domain at the time of its first disclosure to the Receiving Party by the Disclosing Party;

11.1.3 became generally available to the public or otherwise part of the public domain after its disclosure to the Receiving Party by the Disclosing Party and other than through any act or omission of the Receiving Party in breach of this Agreement or the Existing Confidentiality Agreement; or

11.1.4 was disclosed to the Receiving Party, other than under an obligation of confidentiality, by a Third Party who had no obligation to the Disclosing Party not to disclose such information to others.

For the avoidance of doubt, any information obtained by Akcea from PTC, either directly from PTC or by virtue of Akcea's relationship with Ionis Pharmaceuticals, that was considered "Confidential Information" as defined by and pursuant to the Mutual Confidential Disclosure Agreement between Ionis Pharmaceuticals and PTC, dated November 17, 2017 (and as amended from time to time), the "**Existing Confidentiality Agreement**", as of the Effective Date of this Agreement shall be considered Confidential Information of PTC under this Agreement, subject to the provisions of this Article 11.

11.2 Authorized Disclosure. Except as expressly provided otherwise in this Agreement, a Receiving Party may use and disclose Confidential Information of the Disclosing Party as follows: (a) to the extent required to those of its employees, agents and representatives who reasonably need to know such Confidential Information in order to advise or assist the Receiving Party in connection with the performance of its obligations or rights granted or reserved in this Agreement and under appropriate confidentiality provisions no less protective of the Disclosing Party than those set forth in this Agreement; (b) as required by applicable Law; provided, however, that if a Receiving Party is required by Law to make any such disclosure of a Disclosing Party's Confidential Information it will, except where impracticable, give reasonable advance notice to the Disclosing Party of such disclosure requirement, limit disclosure to only the Confidential Information requested to be disclosed and, if requested by the Disclosing Party, cooperate with the Disclosing Party to secure confidential treatment of such Confidential Information required to be disclosed; (c) in communication with existing or prospective investors, lenders, professional advisors, acquirers, merger partners, subcontractors, licensees or Inbound Licensors on a need to know basis, in each case under appropriate confidentiality provisions substantially equivalent to those of this Agreement, except that with respect to any disclosure to an Inbound Licensor, PTC acknowledges that the relevant Inbound Licensor is obligated to retain any information provided to it in confidence only as required pursuant to the terms of the applicable In-License Agreement; or (d) to the extent mutually agreed to in writing by the Parties. The confidentiality and non-use obligations set forth under this Agreement shall survive the termination or expiration of this Agreement for a period of [**].

11.3 Press Release; Disclosure of Agreement.

11.3.1 On or promptly after the Effective Date, the Parties shall jointly issue a press release of the execution of this Agreement in the form mutually agreed by the Parties. Subject to Sections 11.3.2 and 11.4, neither Party may issue any subsequent press release or other public disclosure regarding this Agreement or its terms or the Parties' activities hereunder, or any results or data arising hereunder, except (a) with the other Party's prior consent, or (b) for any disclosure that is reasonably necessary in that Party's sole discretion to comply with applicable securities exchange listing requirements or other applicable Laws. Each Party shall provide to the other Party a copy of any public announcement regarding this Agreement or the subject matter hereof (including any filing with the United States Securities and Exchange Commission (or any stock exchange, including Nasdaq, or any similar regulatory agency in any country other than the United States)), as practicable under the circumstances, reasonably prior to

its scheduled release. Each Party shall have the right to expeditiously review and recommend changes to any such announcement, and, except as otherwise required by securities exchange listing requirements or applicable Law, the Party whose announcement has been reviewed shall remove any Confidential Information of the reviewing Party that the reviewing Party reasonably deems to be inappropriate for disclosure and shall give due consideration to any reasonable comments by the reviewing Party relating to such announcement, including the provisions of this Agreement for which confidential treatment should be sought. At the request of either Party, the other Party will reasonably consider in good faith whether a press release or other public disclosure described in this Section 11.3.1 should be a joint release by both Parties and, in such a case, the Parties will use good faith efforts to mutually agree on the content of any such joint release. Notwithstanding the foregoing, to the extent information regarding this Agreement has already been publicly disclosed, each Party (other than a Party that had caused such information to become publicly disclosed in breach of this ARTICLE 11) may subsequently disclose the same information to the public without the consent of the other Party.

11.3.2 Each Party shall be permitted to disclose the terms of this Agreement, in each case under appropriate confidentiality provisions substantially equivalent to those of this Agreement, to any existing or prospective investors, lenders, professional advisors, acquirers, merger partners, subcontractors, licensees or Inbound Licensors, except that, with respect to any disclosure to an Inbound Licensor that is not Ionis Pharmaceuticals, PTC acknowledges that the relevant Inbound Licensor is obligated to retain any information provided to it in confidence only as required pursuant to the terms of the applicable In-License Agreement.

11.3.3 If either Party proposes to file with the Securities and Exchange Commission or the securities regulators of any state or other jurisdiction a registration statement, periodic report, or any other disclosure document which describes or refers to this Agreement under the Securities Act of 1933, as amended, the Securities Exchange Act, of 1934, as amended, or any other applicable securities Law (collectively, the "**Securities Acts**"), such Party will notify the other Party of such intention and will provide such other Party with a copy of relevant portions of the proposed filing not less than [**] prior to such filing, and will seek to obtain confidential treatment of any information concerning the Agreement that such other Party requests be kept confidential (except to the extent advised by counsel that confidential treatment is not available for such information), and will only disclose Confidential Information which it is advised by counsel is legally required to be disclosed. No such notice will be required under this Section 11.3.3 if the substance of the description of or reference to this Agreement contained in the proposed filing has been included in any previous filing made by either Party hereunder or otherwise approved by the other Party. For clarity, the Parties hereby acknowledge and agree that each Party may file this Agreement under the Securities Acts in the United States and that the Parties shall each use reasonable efforts to obtain confidential treatment for mutually agreed upon portions of this Agreement.

11.4 Publications. Neither Party nor its Affiliates shall publish or publicly disclose the scientific results of any of the activities conducted by the other Party under this Agreement without the prior written consent of the other Party, except as expressly permitted in this Section 11.4. The Parties recognize that it may be useful or required to publish or publicly disclose the results of Exploitation activities conducted hereunder, and each Party (and its Affiliates and sublicensees) shall be free to publish or publicly disclose such results, including on its clinical trials registry or on a government-sponsored database such as www.clinicaltrials.gov, subject to the prior review by the other Party for patentability and protection of its Confidential Information as described in this Section 11.4. The Party that desires to publish such results shall provide the other Party with a copy of such proposed abstract, manuscript, or presentation no less than [**] in the case of abstracts) prior to its intended submission for publication. The reviewing Party shall respond in writing promptly and in no event later than [**] in the case of abstracts) after receipt of the proposed material, with one or more of the following: (a) comments on the proposed material, which the publishing Party shall consider in good faith, (b) a specific statement of concern, based upon the need to seek patent protection or to block publication if the reviewing Party determines that the proposed disclosure contains or describes intellectual property that should be maintained as a trade secret to protect a Compound or a Product or any Exploitation activities conducted under this Agreement, or (c) an identification of the reviewing Party's Confidential Information that is contained in the material reviewed. In the event of concern over patent protection or whether maintaining a trade secret would be a priority, the publishing Party agrees not to submit such publication or to make such presentation that contains such information until the reviewing Party is given a reasonable period of time, and in no event more than [**], to seek patent protection for any material in such publication or presentation which it believes is patentable or to resolve any other issues; *provided*, *however*, that the publishing Party shall abandon such proposed publication or presentation if the reviewing Party reasonably determines in good faith that maintaining such information as a trade secret is a commercially-reasonable priority. Any Confidential Information of the reviewing Party shall, if requested by the reviewing Party, be removed.

11.5 Remedies. Each Party shall be entitled to seek, in addition to any other right or remedy it may have, at Law or in equity, a temporary injunction, without the posting of any bond or other security, enjoining or restraining the other Party from any violation or threatened violation of this ARTICLE 11.

11.6 Acknowledgment. PTC will acknowledge in any press release, public presentation, or publication regarding a Product and intended for or reasonably likely to be the subject of broad distribution that such Product is under license from Akcea and Akcea's stock ticker symbol (*e.g.*, NASDAQ: AKCA). Akcea and Ionis may include any Product in any description of Akcea's and Ionis' drug pipeline. To the extent permitted by Applicable Law, PTC will include the words "*Discovered and developed by Ionis Pharmaceuticals and under license from Akcea Therapeutics*" in relevant scientific, medical and other Product-related communications to the extent such communications address the research, discovery or commercialization of a Product. Notwithstanding the foregoing, PTC shall have no obligation to include such attribution language in any of the following: (a)

communications or materials where such inclusion would be prohibited by Applicable Law or applicable Third Party institutional, corporate, or other policies; (b) communications that PTC does not control, such as publications with non-PTC lead authors; or (c) materials primarily focused on or directed to patients, or other materials in which PTC branding is not prominently featured, *provided that*, in each case, PTC will use reasonable efforts to have such attribution language included in any such communication, consistent with the efforts that PTC uses to have statements regarding its own contributions to the Product included in such communication.

ARTICLE 12
REPRESENTATIONS AND WARRANTIES

12.1 Representations and Warranties of Both Parties. Each Party hereby represents and warrants to the other Party, as of the Effective Date, that:

12.1.1 such Party is duly organized, validly existing and in good standing under the Laws of the jurisdiction of its incorporation and has full corporate power and authority to enter into this Agreement and to carry out the provisions hereof;

12.1.2 such Party has taken all necessary action on its part to authorize the execution and delivery of this Agreement and the performance of its obligations hereunder;

12.1.3 this Agreement has been duly executed and delivered on behalf of such Party, and constitutes a legal, valid, binding obligation, enforceable against it in accordance with the terms hereof;

12.1.4 the execution, delivery and performance of this Agreement by such Party does not conflict with any agreement or any provision thereof, or any instrument or understanding, oral or written, to which it is a party or by which it is bound, nor violate any law or regulation of any court, governmental body or administrative or other agency having jurisdiction over such Party;

12.1.5 no government authorization, consent, approval, license, exemption of or filing or registration with any court or governmental department, commission, board, bureau, agency or instrumentality, domestic or foreign, under any applicable Laws currently in effect, is or will be necessary for, or in connection with, the transaction contemplated by this Agreement or any other agreement or instrument executed in connection herewith, or for the performance by it of its obligations under this Agreement and such other agreements, except as may be required to conduct Clinical Trials, to Manufacture Compounds or Products, or to seek or obtain Regulatory Approvals; and

12.1.6 Such Party is not debarred under the United States Federal Food, Drug and Cosmetic Act or comparable Applicable Laws and it does not, and will not during the Term, employ or use the services of any person or entity that is debarred, in connection with the Development, Manufacture or Commercialization of the Products. If either Party becomes aware of the debarment or threatened debarment of any person or entity providing services to such Party, including the Party itself and its Affiliates or Sublicensees, which directly or indirectly relate to activities under this Agreement, the other Party will be immediately notified in writing.

12.2 Representations, Warranties and Covenants, as applicable, of Akcea. Akcea hereby represents, warrants, and covenants to PTC, as of the Effective Date that:

12.2.1 Akcea has all rights, authorizations and consents necessary to grant all rights and licenses it purports to grant to PTC with respect to the Akcea IP under this Agreement, and has obtained the prior written consent of Ionis Pharmaceuticals as required under the Ionis Pharmaceuticals/Akcea License Agreements with respect to the grant of such rights and licenses.

12.2.2 It has sufficient legal or beneficial title and ownership or right to license (or sublicense as the case may be) with respect to the Akcea IP as is necessary to fulfill its obligations under this Agreement and to grant the licenses (or sublicenses as the case may be) to PTC pursuant to this Agreement.

12.2.3 To the best of its knowledge, no actions, suits, claims, disputes, or proceedings concerning the Akcea IP licensed hereunder are currently pending or are threatened in writing, that if determined adversely to Akcea or Ionis Pharmaceuticals, as applicable, would have an adverse effect on Akcea's ability to grant the licenses (or sublicenses as the case may be) to PTC, or perform its obligations, under this Agreement, or that would have an adverse effect on or would impair PTC's right to practice under the licenses (or sublicenses as the case may be) granted under this Agreement by Akcea to PTC.

12.2.4 All employees and contractors of Akcea and Ionis Pharmaceuticals, as applicable, that are inventors of any of the inventions claimed in the Akcea Patent Rights and that have performed Development or Manufacturing activities on behalf of Akcea or Ionis Pharmaceuticals or their respective Affiliates, as applicable, have entered into written agreements pursuant to which such Persons are obligated to assign all rights, title, and interests in and to any such inventions developed by them, whether or not patentable, to Akcea, Ionis Pharmaceuticals or such Affiliate, respectively, as the sole owner thereof.

12.2.5 To the best of its knowledge, there are no additional licenses (beyond those granted to PTC under this Agreement) under any intellectual property owned or Controlled by Akcea, Ionis Pharmaceuticals or their respective Affiliates that would be required in order for PTC to Develop, Manufacture, or Commercialize the Products in the PTC Territory.

12.2.6 The Akcea IP constitutes all of the Patent Rights and Know-How Controlled by Akcea that are necessary to Develop, Manufacture, and Commercialize the Compounds and the Products as contemplated under this Agreement. Neither Akcea nor Ionis Pharmaceuticals has previously assigned, transferred, conveyed, or otherwise encumbered its rights, title, or interests in or to the Akcea IP in a manner that conflicts with any rights granted to PTC hereunder with respect to the Products.

12.2.7 Schedule 1.4 (Akcea Core Technology Patent Rights), Schedule 1.8 (Akcea Manufacturing Patent Rights), and Schedule 1.13 (Akcea Product-Specific Patent Rights), set forth true, correct, and complete lists of all Akcea Core Technology Patent Rights, all Akcea Product-Specific Patent Rights, and Akcea Manufacturing Patent Rights, respectively, and indicates whether each such Patent Right is owned by Akcea or licensed by Akcea from a Third Party and if so, identifies the licensor or sublicensor from which the Patent Right is licensed. Akcea Controls such Patent Rights and is entitled to grant all rights and licenses (or sublicenses, as the case may be) under such Patent Rights that it purports to grant to Akcea under this Agreement.

12.2.8 To the best of its knowledge, (i) there is no fact or circumstance known by Akcea that would cause Akcea to reasonably conclude that any Akcea Patent Right is invalid or unenforceable; (ii) there is no fact or circumstance known by Akcea that would cause Akcea to reasonably conclude the inventorship of each Akcea Patent Right is not properly identified on each patent; and (iii) all official fees, maintenance fees, and annuities for the Akcea Patent Rights have been paid and all administrative procedures with governmental agencies have been completed. None of the Akcea Patent Rights is currently involved in any interference, reissue, re-examination, *inter partes* review, cancellation, or opposition proceeding and neither Akcea, Ionis Pharmaceuticals nor any of their respective Affiliates, has received any written notice from any Person or has knowledge of such actual or threatened proceeding.

12.2.9 Akcea has set forth on Schedule 1.39 (Existing In-License Agreements) a true, correct, and complete lists of all agreements pursuant to which a Third Party has granted Akcea a license under any Know-How or Patent Rights that is necessary to Develop, Manufacture, or Commercialize the Compounds or the Products in the Territory, and all such Patents and Know-How are Controlled by Akcea and included in the Akcea IP. All Existing In-License Agreements are in full force and effect, and Akcea has provided PTC with true and complete copies of each such Existing In-License Agreements and all amendments thereto. Neither Akcea nor, to the best its knowledge, the counterparty to an Existing In-License Agreement is in default with respect to a material obligation under such Existing In-License Agreement, and neither such party has claimed or has grounds upon which to claim that the other party is in default with respect to a material obligation under any Existing In-License Agreement.

12.2.10 To the best of its knowledge, (i) no issued patent owned by a Third Party will be infringed by the Development, Manufacture (as manufactured by Akcea, Ionis Pharmaceuticals or their respective contract manufacturing organizations (CMOs)), or Commercialization of the Compounds and Products as contemplated by this Agreement in the Territory, and (ii) Akcea, Ionis Pharmaceuticals and their respective Affiliates have not misappropriated any Third Party's Know-How in the course of the Development and Manufacture of the Compounds or the Products.

12.2.11 All Regulatory Approval Applications, and other material regulatory submissions made with any Regulatory Authority relating to the Development, Manufacture, marketing, distribution, or sale of the Products have been provided to PTC in an appropriate electronic format prior to the Effective Date. Except as otherwise disclosed by Akcea to PTC via the electronic data room hosted in connection with the transactions contemplated hereunder, neither Akcea, Ionis Pharmaceuticals nor any of their respective Affiliates or licensees has received any written notice or allegation from any Regulatory Authority regarding (i) any actual, alleged, possible, or potential violation of or failure to comply with any Applicable Law, or (ii) any actual, proposed, or potential revocation, withdrawal, suspension, cancellation, termination, or modification of any regulatory filing for the Products, and to Akcea's knowledge there is no reasonable basis for any such notice or allegation.

12.2.12 All Development of the Compounds and the Products has been conducted, in all material respects, in accordance with all applicable Law. There is no legal proceeding pending or, to Akcea' knowledge, threatened, by any Regulatory Authority to suspend, investigate, or terminate Development of any Compound or Product.

12.2.13 To the best of Akcea's knowledge, true, complete and correct copies of all material information with respect to the safety and efficacy of the Compounds and/or the Products have been provided to PTC.

12.3 Covenants of Akcea. From and after the Effective Date through the expiration or earlier termination of this Agreement, Akcea hereby covenants to PTC that, except as expressly permitted under this Agreement:

12.3.1 Updates to Schedules. Upon PTC's reasonable written request (such request not to be submitted to Akcea more than [**]), Akcea will promptly update Schedule 1.4 (Akcea Core Technology Patent Rights), Schedule 1.8 (Akcea Manufacturing Patent Rights) and Schedule 1.13 (Akcea Product-Specific Patent Rights), and submit such amended Schedules to PTC.

12.3.2 In-Licenses. Akcea and its Affiliates, as applicable, will at all times have obtained the necessary consents from the Inbound Licensors under the In-License Agreements to enter into this Agreement and to grant the licenses to PTC hereunder, and shall provide to PTC, upon PTC's request, written evidence of same. Akcea will not, and will cause its Affiliates not to amend, modify, terminate, or waive any rights under any Existing In-License Agreement or Future In-License Agreement in a manner that would adversely affect PTC's rights or obligations under this Agreement without PTC's prior written consent. Akcea will not, and will cause its Affiliates not to, commit any acts or permit the occurrence of any omissions that would cause or result in the termination of any Existing In-License Agreement or Future In-License Agreement in its entirety or with respect to any rights under such agreement for which such termination would adversely affect PTC's rights or obligations under this Agreement. Akcea will notify PTC in writing within [**] after any such termination of any Existing In-License Agreement or Future In-License Agreement.

12.3.3 Conflicting Agreements. Akcea will not enter into any agreement or other obligation with any Third Party, or amend an existing agreement with a Third Party, in each case, that restricts, limits, encumbers, or conflicts with the rights granted to PTC under this Agreement.

12.3.4 Assignment of Inventions. Akcea shall ensure that all employees and contractors of Akcea and/or Ionis Pharmaceuticals performing Development activities under the Ionis Pharmaceuticals/Akcea License Agreements or this Agreement on behalf of PTC will be obligated to assign all rights, title, and interests in and to any inventions developed by them, whether or not patentable, to Akcea, Ionis Pharmaceuticals or such Affiliate, respectively, as the sole owner thereof.

12.4 Covenants of PTC. From and after the Effective Date through the expiration or earlier termination of this Agreement, PTC hereby covenants to Akcea that, except as expressly permitted under this Agreement, PTC shall ensure that all employees and contractors of PTC performing Development or Commercial activities under this Agreement on behalf of PTC will be obligated to assign all rights, title, and interests in and to any inventions developed by them, whether or not patentable, to PTC or its Affiliate, respectively, as the sole owner thereof.

12.5 Disclaimer. EXCEPT AS OTHERWISE EXPRESSLY SET FORTH IN THIS AGREEMENT, NEITHER PARTY MAKES ANY REPRESENTATION OR EXTENDS ANY WARRANTY OF ANY KIND, EITHER EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY THAT ANY PATENTS ARE VALID OR ENFORCEABLE, AND EXPRESSLY DISCLAIMS ALL IMPLIED WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE AND NONINFRINGEMENT.

ARTICLE 13
INDEMNIFICATION; INSURANCE

13.1 Indemnification by PTC. PTC shall defend, and indemnify and hold harmless, Akcea and its Affiliates and their respective directors, officers, employees, subcontractors, agents and representatives (collectively, the "**Akcea Indemnified Parties**"), from and against any and all liabilities, damages, losses, costs and expenses, including the reasonable fees of attorneys (collectively, "**Losses**"), to the extent arising out of or resulting from any Third Party suits, claims, actions, proceedings or demands ("**Third Party Claims**") to the extent based upon:

13.1.1 any breach of any representation, warranty or covenant made by PTC in this Agreement;

13.1.2 the Development, Manufacture, Commercialization or other Exploitation of a Compound or Product by PTC or its Affiliates or its Sublicensees in the PTC Territory; or

13.1.3 the gross negligence, recklessness, or willful misconduct by PTC or any of the PTC Indemnified Parties;

provided that, in the case of each of Sections 13.1.1-13.1.3 above, PTC shall not be obliged to so defend, and indemnify and hold harmless, the Akcea Indemnified Parties for any Claims to the extent that Akcea has an obligation to indemnify the PTC Indemnified Parties under Section 13.2.

13.2 Indemnification by Akcea. Akcea shall defend, and indemnify and hold harmless, PTC and its Affiliates and Sublicensees and their respective directors, officers, employees, subcontractors, agents and representatives (collectively, the "**PTC Indemnified Parties**"), from and against any and all Losses, to the extent arising out of or resulting from any Third Party Claims to the extent based upon:

13.2.1 any breach of any representation, warranty or covenant made by Akcea in this Agreement;

13.2.2 the Development, Manufacture, Commercialization or other Exploitation of a Compound or Product by Akcea, Ionis Pharmaceuticals or their respective Affiliates or Sublicensees; or

13.2.3 the gross negligence, recklessness, or willful misconduct by Akcea or any of the Akcea Indemnified Parties;

provided that, in the case of each of Sections 13.2.1-13.2.3 above, Akcea shall not be obliged to so defend, and indemnify and hold harmless, the PTC Indemnified Parties for any Claims to the extent that PTC has an obligation to indemnify the Akcea Indemnified Parties under Section 13.1.

13.3 Procedure. A Person entitled to indemnification under this ARTICLE 13 (an "**Indemnified Party**") shall give prompt written notification to the Person from whom indemnification is sought (the "**Indemnifying Party**") of the commencement of any Third Party Claim for which indemnification may be sought or, if earlier, upon the assertion of any such Third Party Claim (it being understood and agreed, however, that the failure by an Indemnified Party to give notice of a Third Party Claim as provided in this Section 13.3 shall not relieve the Indemnifying Party of its indemnification obligation under this Agreement except and only to the extent that such Indemnifying Party is actually damaged as a result of such failure to give notice). Within [**] after delivery of such notification, the Indemnifying Party may, upon written notice thereof to the Indemnified Party, assume control of the defense of such Third Party Claim with counsel reasonably satisfactory to the Indemnified Party. If the Indemnifying Party does not assume control of such defense, the Indemnified Party shall control such defense and, without limiting the Indemnifying Party's indemnification obligations, the Indemnifying Party shall reimburse the Indemnified Party for all costs and expenses, including attorney fees, incurred by the Indemnified Party in defending itself within [**] after receipt of any invoice therefor from the Indemnified Party. The Party not controlling such defense may participate therein at its own expense; *provided that*, if the Indemnifying Party assumes control of such defense and the Indemnified Party in good faith concludes, based on advice from counsel, that the Indemnifying Party and the Indemnified Party have conflicting interests with respect to such Third Party Claim, the Indemnifying Party shall be responsible for the reasonable fees and expenses of counsel to the Indemnified Party in connection therewith. The Party controlling such defense shall keep the other Party advised of the status of such Third Party Claim and the defense thereof and shall consider recommendations made by the other Party with respect thereto. The Indemnified Party shall not agree to any settlement of such Third Party Claim without the prior written consent of the Indemnifying Party, which shall not be unreasonably withheld, delayed or conditioned. The Indemnifying Party shall not, without the prior written consent of the Indemnified Party, agree to any settlement of such Third Party Claim or consent to any judgment in respect thereof that does not include a complete and unconditional release of the Indemnified Party from all liability with respect thereto, that imposes any liability or obligation on the Indemnified Party or that acknowledges fault by the Indemnified Party.

13.4 Insurance. Each Party shall maintain, at its own cost, insurance against liability and other risks associated with its activities and obligations under this Agreement, including its Development, Manufacturing, Commercialization and other Exploitation activities, as applicable, and its indemnification obligations hereunder, in such amounts, subject to such deductibles and on such terms as are reasonable for a company such as such Party for the activities to be conducted by it under this Agreement. Each Party shall promptly furnish to the other Party evidence of such insurance upon request.

13.5 Limitation of Liability. EXCEPT FOR (A) A BREACH OF SECTION 7.1.1, (B) A BREACH OF ARTICLE 11, (C) CLAIMS OF A THIRD PARTY THAT ARE SUBJECT TO INDEMNIFICATION UNDER THIS ARTICLE 13, OR (D) A BREACH OF SECTION 14.3.1, NEITHER AKCEA NOR PTC, NOR ANY OF THEIR RESPECTIVE AFFILIATES, LICENSORS, LICENSEES OR SUBLICENSEES, WILL BE LIABLE TO THE OTHER PARTY, ITS AFFILIATES OR SUBLICENSEES FOR ANY INDIRECT, INCIDENTAL, CONSEQUENTIAL, SPECIAL OR PUNITIVE DAMAGES OR LOST PROFITS OR ROYALTIES, LOST DATA OR COST OF PROCUREMENT OF SUBSTITUTE GOODS OR SERVICES, WHETHER LIABILITY IS ASSERTED IN CONTRACT, TORT (INCLUDING NEGLIGENCE AND STRICT PRODUCT LIABILITY), INDEMNITY OR CONTRIBUTION, AND IRRESPECTIVE OF WHETHER THAT PARTY OR ANY REPRESENTATIVE OF THAT PARTY HAS BEEN ADVISED OF, OR OTHERWISE MIGHT HAVE ANTICIPATED THE POSSIBILITY OF, ANY SUCH LOSS OR DAMAGE.

ARTICLE 14
TERM AND TERMINATION

14.1 Term. This Agreement shall commence as of the Effective Date and, unless terminated earlier, this Agreement shall continue in full force and effect until the expiration of the last to expire Royalty Term with respect to all Products in all countries in the PTC Territory (the "**Term**").

14.2 Termination. This Agreement may be terminated at any time upon written notice by either Party if the other Party is in material breach of its obligations hereunder and has not cured such breach within thirty (30) days in the case of a payment breach, or within sixty (60) days in the case of all other breaches, after the non-breaching Party has provided written notice to the breaching Party of such breach.

14.3 Effects of Termination. Without limiting any other legal or equitable remedies that either Party may have, if this Agreement expires or is terminated for any reason then the following shall occur:

14.3.1 the license grants to PTC shall terminate immediately, and PTC, its Affiliates and Sublicensees will cease selling the applicable Products; *provided*, *however*, that (i) PTC may sell existing inventory for up to [**], and (ii) Akcea may elect in its sole discretion to have PTC continue to sell the applicable Products as part of any orderly transition of contemplated by the provisions of this Section 14.3;

14.3.2 PTC shall, and hereby does, grant to Akcea a perpetual, irrevocable, transferable, sublicensable (through multiple tiers) license under the PTC IP to Exploit Compounds and Products in the PTC Territory; such license shall be exclusive with respect to the PTC Product-Specific IP and nonexclusive with respect to the PTC Background Know-How and the PTC Background Patent Rights, and shall be royalty-free and fully-paid-up with respect to any Compound or Product;

14.3.3 if Akcea so requests, and to the extent permitted under the relevant agreement at the time of termination, PTC shall transfer to Akcea any agreements between PTC or any of its Affiliates, on the one hand, and any Affiliate or Third Party, on the other hand, to the extent relating to the Exploitation of any Compound or Product in the Territory to which PTC or any of its Affiliates is a party, subject to any required consents of such Third Party, which PTC shall use commercially reasonable efforts to obtain promptly;

14.3.4 PTC shall provide to Akcea a fair and accurate description of the status of the Exploitation of such Compounds and Products in the Territory through the effective date of termination or expiration;

14.3.5 PTC shall promptly transfer to Akcea or Akcea's designee (i) possession and ownership of all Regulatory Filings, Regulatory Approvals and pricing and reimbursement approvals relating to the Exploitation of the Compounds and Products, (ii) copies of all data, reports, records and materials, and other sales and marketing related information in PTC's possession or Control to the extent that such data, reports, records, materials or other information relate to the Exploitation of any of such Compounds and Products, including all non-clinical and clinical data relating to any of such Compounds and Products, and customer lists and customer contact information and all adverse event or other safety data in the possession or Control of PTC, any of its Affiliates or any Sublicensee; *provided that* PTC shall use commercially reasonable efforts to obtain for Akcea the right to access all such data, reports, records, materials, and other sales and marketing related information, and (iii) all records and materials containing Confidential Information of Akcea. PTC shall further appoint, and ensure that its Affiliates and the Sublicensees appoint, Akcea as the agent for PTC, its Affiliates and the Sublicensees for all matters relating to such Products and Compounds involving Regulatory Authorities in the Territory until all Regulatory Approvals and other Regulatory Filings have been transferred to Akcea or its designee;

14.3.6 if the effective date of termination or expiration is after the First Commercial Sale of a Product in any country in the PTC Territory, then PTC shall appoint Akcea or its designee as the exclusive distributor of the Product in the Territory and grant Akcea the right to appoint sub-distributors, until such time as all Regulatory Approvals and pricing and reimbursement approvals in the Territory have been transferred to Akcea or its designee;

14.3.7 PTC shall promptly transfer and assign to Akcea all of PTC's, its Affiliates' and any Sublicensee's rights, title and interests in and to all Product Trademarks used in the Commercialization of such Compounds and Products (but not any

house marks of such Person or any trademark containing the word "PTC" owned by PTC or any of its Affiliates or any Sublicensee);

14.3.8 PTC shall, upon Akcea's written request, transfer to Akcea any inventory of such Compounds and Products owned or controlled by PTC, any of its Affiliates or any Sublicensee as of the termination date at the actual price paid by PTC, such Affiliate or such Sublicensee for such supply;

14.3.9 PTC shall provide any other assistance reasonably requested by Akcea for the purpose of allowing Akcea or its designee to proceed expeditiously with the Exploitation of the Compounds and Products in the Territory; and

14.3.10 PTC shall, and shall ensure that its Affiliates and the Sublicensees shall, execute all documents and take all such further actions as may be reasonably requested by Akcea in order to give effect to the foregoing clauses.

14.4 Accrued Rights; Surviving Provisions of the Agreement.

14.4.1 Termination or expiration of this Agreement for any reason shall be without prejudice to any rights that shall have accrued to the benefit of any Party prior to such termination or expiration, including the payment obligations under ARTICLE 9 hereof, and any and all damages or remedies arising from any breach hereunder. Such termination or expiration shall not relieve any Party from obligations which are expressly indicated to survive expiration or termination of this Agreement.

14.4.2 The provisions of ARTICLE 1 (Definitions), ARTICLE 11 (Confidentiality), ARTICLE 13 (Indemnification; Insurance), ARTICLE 14 (Term and Termination) and ARTICLE 15 (Miscellaneous) and Section 6.3 (Effect of Termination on Sublicenses), Section 6.5 (Licenses to Akcea), Section 6.6 (No Other Rights), Section 6.7 (Section 365(n) of the Bankruptcy Code), Section 9.8 (Accounting), Section 9.10 (Taxes), Section 9.11 (Currency Exchange), Section 10.1 (Ownership of Inventions: Disclosure), and Section 12.5 (Disclaimer) shall survive the termination of this Agreement in its entirety or expiration of this Agreement for any reason, in accordance with their respective terms and conditions, and for the duration stated, and where no duration is stated, shall survive indefinitely.

ARTICLE 15
MISCELLANEOUS

15.1 Governing Law. This Agreement and any dispute arising from the performance or breach hereof shall be governed by and construed and enforced in accordance with the Laws of the State of New York without reference to conflicts of laws principles; provided that with respect to matters involving the enforcement of intellectual property rights, the Laws of the applicable country shall apply. The provisions of the United Nations Convention on Contracts for the International Sale of Goods shall not apply to this Agreement or any subject matter hereof.

15.2 Dispute Resolution. The Parties agree to attempt in good faith to promptly resolve any dispute, controversy, or claim ("**Dispute**") arising out of or relating to this Agreement through negotiations between the Parties before resorting to other remedies available to them. If the Parties are unable to resolve the Dispute and any Party wishes to pursue its rights relating to such Dispute, then, except as otherwise expressly provided in this Agreement, the relevant Party shall first submit the dispute to mediation within [**] after written notice by one Party to the other demanding non-binding mediation. Each of the Parties hereby agrees that any mediation shall be handled by a mediator appointed by Judicial Arbitration and Mediation Services, Inc. ("**JAMS**") in New York, New York, United States. All parties to any mediated Dispute shall share the costs of the mediation equally, except that each party to the Dispute shall bear its own costs and expenses, including attorney's fees, witness fees, travel expenses, and preparation costs. If the Dispute is not resolved through mediation, the Dispute shall be submitted to arbitration in New York, New York by a single arbitrator; provided, that if any Party that is a party to the Dispute cannot agree on a single arbitrator within [**] of the submission to arbitration, the matter shall be submitted to JAMS in New York, New York for arbitration before a single arbitrator from the JAMS list, and pursuant to the JAMS Comprehensive Arbitration Rules and Procedures. All parties to any arbitrated Dispute shall share the costs of the arbitration equally, except that a party to the Dispute shall bear its own costs and expenses, including attorney's fees, witness fees, travel expenses, and preparation costs. Every aspect of the arbitration, including the award, shall be treated as confidential information. The arbitrator's award shall be final and binding upon the Parties that are party to the Dispute, and judgment upon the award may be entered in any state or federal court of competent jurisdiction in New York State, or application may be made to such court for a judicial acceptance of the award and an enforcement as the law of such jurisdiction may require or allow. Nothing herein shall restrict the ability of any Party to provide factual testimony during such proceedings. Notwithstanding the foregoing, any Party may seek an injunction or other equitable relief pending arbitration from any federal or state court of competent jurisdiction in New York State. The forbearance to enforce an agreement to arbitrate shall not constitute a waiver of any rights under this Agreement except to the extent stated in this Agreement.

15.3 Assignment.

15.3.1 This Agreement may not be assigned or otherwise transferred, nor may any right or obligation hereunder be assigned or transferred, by either Party without the written consent of the other Party; *provided, however*, that either Party may, without the other Party's written consent, assign this Agreement and its rights and obligations hereunder in whole or in part to (a) an Affiliate; or (b) the Acquirer in the context of a Change of Control; *provided, further* if PTC transfers or assigns this Agreement

to one of its Affiliates that is incorporated in a jurisdiction that does not have a Bilateral Income Tax Treaty with the United States or in a jurisdiction where a Bilateral Income Tax Treaty requires withholding taxes on any payment described in this Agreement, then PTC (or such Affiliate), will increase (*i.e.*, "*gross up*") any payment due Akcea under ARTICLE 9 for the Incremental Tax Cost such that Akcea receives the amount Akcea would have otherwise received under ARTICLE 9 but for PTC's transfer or assignment. Any purported assignment in violation of this Section 15.3.1 shall be void.

The "**Incremental Tax Cost**" will equal the amount of IRC Sec 901 (or successor provision) taxes withheld under ARTICLE 9 in each year in which such tax is paid and Akcea cannot obtain a corresponding cash benefit from the foreign tax credit, grossed up by the applicable withholding tax rate based on a payment to a United States Person (unless the actual applicable treaty is lower, in which case the lower withholding tax rate will be used) to equal the pre withholding tax payment.

To the extent Akcea utilizes a [**] in any year, Akcea will [**] PTC an amount equal to (i) [**]% of the [**] or (ii) [**] Akcea resulting from the [**], which [**] will be calculated as the [**]. To assist PTC in determining when a [**] from Akcea pursuant to the foregoing sentence, beginning with the first Annual tax return for the year in which PTC [**] (*i.e.*, "*[**]*") payment under this Section 15.3.1, and each year thereafter (including, for clarity, all years in which Akcea [**] or [**]), Akcea will provide PTC with Akcea's Annual tax returns (federal and state) and, in years in which Akcea utilizes the [**], supporting documentation for such [**]. Notwithstanding the foregoing, if any increase in the applicable withholding tax is in any way a result of the transfer or assignment by Akcea of any intellectual property or a portion of the rights under this license outside of the United States, PTC will not be obligated to [**] any [**] to the extent such transfer or assignment by Akcea caused such increase in the withholding tax.

15.3.2 In the case of PTC, an Acquirer of PTC must certify to Akcea within [**] after the closing date of the Change of Control transaction, its intent to continue the Commercialization of the Compounds and the Products in accordance with the PTC Commercialization Plan. In the case of Akcea, an Acquirer of Akcea must certify to PTC within [**] after the closing date of the Change of Control transaction, its intent to continue the Commercialization of the Compounds and the Products in accordance with the then-current commercialization plan under the Ionis Pharmaceuticals/Akcea License Agreements. The Acquirer and the other Party may enter into a written agreement containing additional provisions to ensure that such Change of Control does not delay the receipt of Regulatory Approval or Commercialization of the Compounds and the Products in the PTC Territory.

15.3.3 Each Party agrees that, notwithstanding any provision of this Agreement to the contrary, if a Party undergoes a Change of Control, no Patent Right, Know-How or other intellectual property or other proprietary rights that were not Controlled prior to such Change of Control by such Party or by any of its Affiliates who were its Affiliates prior to such Change of Control (such Party's "**Pre-Existing Affiliates**") will be deemed Controlled by such Party or its Affiliates for purposes of this Agreement after such Change of Control.

15.3.4 No Reach-Through. Notwithstanding anything to the contrary set forth herein, but subject to the Exclusive License and the reserved rights under Sections 6.1 and 6.5, (a) in the event of a Change of Control of a Party, this Agreement shall not be deemed to prevent or prohibit the Acquirer or any of its Affiliates (other than such Party and its Pre-Existing Affiliates) from Exploiting any compounds or products in the PTC Territory (other than the Party and its Pre-Existing Affiliates) or granting any Third Party any right or licenses to do so; and (b) in the event that Akcea acquires (whether by way of merger, acquisition, purchase of all or substantially all of the relevant business or assets, or otherwise) a Third Party (the "**Acquired Third Party**"), this Agreement shall not be deemed to prevent or prohibit the Acquired Third Party from Exploiting any compounds or products in the PTC Territory or from granting any Third Party any right or license to do so.

15.4 Performance by Affiliates. Each Party hereby acknowledges and agrees that it shall be responsible for the full and timely performance as and when due under, and observance of all the covenants, terms, conditions and agreements set forth in this, Agreement by its Affiliate(s).

15.5 Force Majeure. No Party shall be held liable or responsible to the other Party nor be deemed to be in default under, or in breach of any provision of, this Agreement for failure or delay in fulfilling or performing any obligation (other than a payment obligation) of this Agreement when such failure or delay is due to force majeure. For purposes of this Agreement, force majeure is defined as any cause beyond the control of the affected Party and without the fault or negligence of such Party, which may include acts of God; material changes in Law; war; civil commotion; destruction of production facilities or materials by fire, flood, earthquake, explosion or storm; labor disturbances; epidemic; and failure of public utilities or common carriers. In such event the Party affected by such force majeure shall immediately notify the other Party of such inability and of the period for which such inability is expected to continue. The Party giving such notice shall thereupon be excused from such of its obligations under this Agreement as it is thereby disabled from performing for so long as it is so disabled for up to a maximum of [**], after which time the Parties shall promptly meet to discuss in good faith how to best proceed in a manner that maintains and abides by the Agreement. To the extent possible, each Party shall use reasonable efforts to minimize the duration of any force majeure.

15.6 Notices. Any notice or request required or permitted to be given under or in connection with this Agreement shall be deemed to have been sufficiently given if in writing and personally delivered or sent by certified mail (return receipt requested), facsimile transmission (receipt verified), or overnight express courier service (signature required), prepaid, to the Party for which such notice is intended, at the address set forth for such Party below:

If to PTC,

addressed to: PTC Therapeutics International Limited
5th Floor
3 Grand Canal Plaza
Grand Canal Street Upper
Dublin 4
D04 EE70
Attention: Legal Department
Telephone: + 353-1-906-8700
Email: [**]

with a copy to: Wilmer Cutler Pickering Hale and Dorr LLP
7 World Trade Center
250 Greenwich Street
New York, NY 10007
Attention: Steven D. Singer
Telephone: 212-295-6307
Facsimile: 212-230-8888

If to Akcea,

addressed to: Akcea Therapeutics, Inc.
22 Boston Wharf Road
Boston, Massachusetts 02210
Attention: Chief Executive Officer
Telephone: 617-217-0202
Facsimile: [**]

with a copy to: Akcea Therapeutics, Inc.
22 Boston Wharf Road
Boston, Massachusetts 02210
Attention: Vice President, Legal

Telephone: [**]
Email: [**]

or to such other address for such Party as it shall have specified by like notice to the other Party, *provided that* notices of a change of address shall be effective only upon receipt thereof. If delivered personally or by facsimile transmission, the date of delivery shall be deemed to be the date on which such notice or request was given. If sent by overnight express courier service, the date of delivery shall be deemed to be the next Business Day after such notice or request was deposited with such service. If sent by certified mail, the date of delivery shall be deemed to be the third (3rd) Business Day after such notice or request was deposited with the U.S. Postal Service.

15.7 Export Clause. Each Party acknowledges that the Laws of the United States restrict the export and re-export of commodities and technical data of United States origin. Each Party agrees that it will not export or re-export restricted commodities or the technical data of the other Party in any form without the appropriate United States and foreign government licenses.

15.8 Waiver. Neither Party may waive or release any of its rights or interests in this Agreement except in writing. The failure of either Party to assert a right hereunder or to insist upon compliance with any term of this Agreement shall not constitute a waiver of that right or excuse a similar subsequent failure to perform any such term or condition. No waiver by either Party of any condition or term in any one or more instances shall be construed as a continuing waiver of such condition or term or of another condition or term except to the extent set forth in writing.

15.9 Severability. If any provision hereof should be invalid, illegal or unenforceable in any jurisdiction, the Parties shall negotiate in good faith a valid, legal and enforceable substitute provision that most nearly reflects the original intent of the Parties and all other provisions hereof shall remain in full force and effect in such jurisdiction and shall be liberally construed in order to carry out the intentions of the Parties as nearly as may be possible. Such invalidity, illegality or unenforceability shall not affect the validity, legality or enforceability of such provision in any other jurisdiction.

15.10 Entire Agreement. This Agreement, together with the Schedules hereto, set forth all the covenants, promises, agreements, warranties, representations, conditions and understandings between the Parties and supersede and terminate all prior agreements and understanding between the Parties. In particular, and without limitation, this Agreement supersedes and replaces any and all term sheets relating to the transactions contemplated by this Agreement and exchanged between the Parties prior to the Effective Date. There are no covenants, promises, agreements, warranties, representations, conditions or understandings, either oral or written, between the Parties other than as set forth herein. No subsequent alteration, amendment, change or addition to this

Agreement shall be binding upon the Parties unless reduced to writing and signed by the respective authorized officers of the Parties.

15.11 Independent Contractors. Nothing herein shall be construed to create any relationship of employer and employee, agent and principal, partnership or joint venture between the Parties. Each Party is an independent contractor. Neither Party shall assume, either directly or indirectly, any liability of or for the other Party. Neither Party shall have the authority to bind or obligate the other Party and neither Party shall represent that it has such authority.

15.12 Headings; Construction; Interpretation. Headings and any table of contents used herein are for convenience only and shall not in any way affect the construction of or be taken into consideration in interpreting this Agreement. The terms of this Agreement represent the results of negotiations between the Parties and their representatives, each of which has been represented by counsel of its own choosing, and neither of which has acted under duress or compulsion, whether legal, economic or otherwise. Accordingly, the terms of this Agreement shall be interpreted and construed in accordance with their usual and customary meanings, and each of the Parties hereby waives the application in connection with the interpretation and construction of this Agreement of any rule of Law to the effect that ambiguous or conflicting terms or provisions contained in this Agreement shall be interpreted or construed against the Party whose attorney prepared the executed draft or any earlier draft of this Agreement. Any reference in this Agreement to an Article, Section, subsection, paragraph, clause or Schedule shall be deemed to be a reference to any Article, Section, subsection, paragraph, clause or Schedule, of or to, as the case may be, this Agreement. Except where the context otherwise requires, (a) any definition of or reference to any agreement, instrument or other document refers to such agreement, instrument other document as from time to time amended, supplemented or otherwise modified (subject to any restrictions on such amendments, supplements or modifications set forth herein or therein), (b) any reference to any Law refers to such Law includes all rules and regulations thereunder and any successor Law, in each case as from time to time enacted, repealed or amended, (c) the words “herein,” “hereof” and “hereunder,” and words of similar import, refer to this Agreement in its entirety and not to any particular provision hereof, (d) the words “include,” “includes,” “including” shall be deemed to be followed by the phrase “but not limited to,” “without limitation” or words of similar import, (e) the word “or” is used in the inclusive sense (and/or), (f) words in the singular or plural form include the plural and singular form, respectively, (g) references to any gender refer to each other gender, (h) references to a particular Person include such Person’s successors and assigns to the extent not prohibited by this Agreement, and (i) a capitalized term not defined herein but reflecting a different part of speech than a capitalized term which is defined herein shall be interpreted in a correlative manner.

15.13 Books and Records. Any financial books and records to be maintained under this Agreement by a Party or its Affiliates or Sublicensees shall be maintained in accordance with U.S. generally accepted accounting principles (“**GAAP**”) or International Financial Reporting Standards, as applicable.

15.14 Further Actions. Each Party shall execute, acknowledge and deliver such further instruments, and do all such other acts, as may be necessary or appropriate in order to carry out the expressly stated purposes and the clear intent of this Agreement.

15.15 Parties in Interest. All of the terms and provisions of this Agreement shall be binding upon, and shall inure to the benefit of and be enforceable by the parties hereto and their respective successors, heirs, administrators and permitted assigns.

15.16 Counterparts. This Agreement may be signed in counterparts, each and every one of which shall be deemed an original, notwithstanding variations in format or file designation which may result from the electronic transmission, storage and printing of copies from separate computers or printers. Facsimile signatures and signatures transmitted via PDF shall be treated as original signatures.

[*Signature page to follow****]***

IN WITNESS WHEREOF, and intending to be legally bound hereby, the Parties have caused this Agreement to be executed by their duly authorized representatives as of the Effective Date.

Akcea Therapeutics, Inc.

By:/s/ Paula Soteropoulos

Name: Paula Soteropoulos

Title: Chief Executive Officer

PTC Therapeutics International Limited

By: /s/ Adrian Haigh

Name: Adrian Haigh

Title: Director

SCHEDULE 1.4

Akcea Core Technology Patent Rights

Ionis Docket Number	Country/Treaty	Application/ Patent Number	Filing Date	Title	Grant Date
[**]	[**]	[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]	[**]	[**]

Schedule 1.8

Akcea Manufacturing Patent Rights

Technology	Ionis Docket Number	Country/Treaty	Application/Patent Number	Filing Date	Title
[**]	[**]	[**]	[**]	[**]	[**]

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 2 pages were omitted. [**]

Schedule 1.13

Akcea Product-Specific Patent Rights

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Ionis Docket No.	Country	Application/ Patent No.	Filing Date	Grant Date	Title
[**]	[**]	[**]	[**]	[**]	[**]

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 5 pages were omitted. [**]

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Ionis Docket No.	Country	Application/ Patent No.	Filing Date	Grant Date	Title
[**]	[**]	[**]	[**]	[**]	[**]

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 19 pages were omitted. [**]

Schedule 1.39

Existing In-License Agreements

[**]

In each case, only if (and to the extent) a Product under this Agreement incorporates technology that is in-licensed by Akcea or Ionis Pharmaceuticals under such agreement.

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 5, 2018

By: /s/ STUART W. PELTZ

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

Exhibit 31.2

CERTIFICATIONS

I, Christine Utter, 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 5, 2018

By: /s/ CHRISTINE UTTER

Christine Utter
Principal 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, 2018 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 5, 2018

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, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Christine Utter, Principal 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 5, 2018

By: /s/ CHRISTINE UTTER

Christine Utter
Principal Financial Officer
(Principal Financial and Accounting Officer)