UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, DC 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 June 30, 2017

OR

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

For the transition period from to

Commission file number 0-19125

Akcea Therapeutics, Inc.

(Exact name of Registrant as specified in its charter)

Delaware	**47-2608175**
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)

55 Cambridge Parkway, Suite 100, Cambridge, MA 02142
(Address of principal executive offices, including zip code)

617-207-0202
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act: **None**

Securities registered pursuant to Section 12(g) of the Act:

Common Stock, $.001 Par Value

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☐ No ☒

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company 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 ☒ (Do not check if a smaller reporting company)	Smaller reporting company ☐
	Emerging growth company ☒

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12(b)-2 of the Securities Exchange Act of 1934). Yes ☐ No ☒

The number of shares of common stock outstanding as of August 2, 2017 was 66,541,629.

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TRADEMARKS

Akcea Therapeutics™ is a trademark of Ionis Pharmaceuticals, Inc.

Ionis Pharmaceuticals™ is a trademark of Ionis Pharmaceuticals, Inc.

AKCEA THERAPEUTICS, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share data)

	June 30, 2017 (Unaudited)	December 31, 2016
ASSETS		
Current assets:		
Cash and cash equivalents	$ 75,445	$ 7,857
Short-term investments	43,223	—
Other current assets	3,939	1,209
Total current assets	122,607	9,066
Property, plant and equipment, net	114	177
Licenses, net	1,281	1,341
Deposits and other assets	102	100
Total assets	$ 124,104	$ 10,684
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 143	$ 476
Payable to Ionis Pharmaceuticals, Inc.	11,244	24,355
Accrued compensation	1,252	2,505
Accrued liabilities	2,213	1,041
Current portion of deferred revenue	54,155	—
Current portion of deferred rent	40	33
Total current liabilities	69,047	28,410
Long-term portion of deferred rent	18	21
Line of credit with Ionis Pharmaceuticals, Inc.	107,507	—
Long-term portion of deferred revenue	30,515	—
Total liabilities	207,087	28,431
Stockholders' equity (deficit):		
Series A convertible preferred stock, $0.001 par value; 28,884,540 shares authorized, issued and outstanding at June 30, 2017 and December 31, 2016, respectively; aggregate liquidation value of $628,613 and $610,304 as of June 30, 2017 and December 31, 2016, respectively	100,000	100,000
Common stock, $0.001 par value; 100,000,000 shares authorized and 0 shares issued and outstanding at June 30, 2017 and December 31, 2016, respectively	—	—
Additional paid-in capital	64,059	56,936
Accumulated other comprehensive loss	(84)	(21)
Accumulated deficit	(246,958)	(174,662)
Total stockholders' equity (deficit)	(82,983)	(17,747)
Total liabilities and stockholders' equity (deficit)	$ 124,104	$ 10,684

See accompanying notes.

AKCEA THERAPEUTICS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except for share and per share data)
(Unaudited)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	**2016**	**2017**	**2016**
Revenue:				
Research and development revenue under collaborative agreements	$ 14,128	$ —	$ 23,725	$ —
Total revenue	14,128	—	23,725	—
Expenses:				
Research and development	18,487	10,944	83,282	22,734
General and administrative	6,915	2,762	11,590	7,014
Total operating expenses	25,402	13,706	94,872	29,748
Loss from operations	(11,274)	(13,706)	(71,147)	(29,748)
Other income (expense):				
Investment income	295	91	358	177
Interest expense	(965)	—	(1,507)	—
Net loss	$ (11,944)	$ (13,615)	$ (72,296)	$ (29,571)
Net loss per share of preferred stock, basic and diluted	$ (0.41)	$ (0.47)	$ (2.50)	$ (1.02)
Weighted-average shares of preferred stock outstanding, basic and diluted	28,884,540	28,884,540	28,884,540	28,884,540

See accompanying notes.

AKCEA THERAPEUTICS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(in thousands)
(Unaudited)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	**2016**	**2017**	**2016**
Net loss	$ (11,944)	$ (13,615)	$ (72,296)	$ (29,571)
Unrealized gains (losses) on investments, net of tax	1	13	(27)	83
Currency translation adjustment	(42)	—	(36)	—
Comprehensive loss	(11,985)	(13,602)	(72,359)	(29,488)

See accompanying notes.

AKCEA THERAPEUTICS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)
(Unaudited)

	Six Months Ended June 30,	
	2017	**2016**
Operating activities:		
Net loss	$ (72,296)	$ (29,571)
Adjustments to reconcile net loss provided by (used in) operating activities:		
Depreciation	56	3
Amortization of licenses	60	60
Amortization of premium on investments, net	139	94
Non-cash interest expense for line of credit with Ionis Pharmaceuticals, Inc.	1,507	—
Non-cash sublicensing expense	33,394	—
Stock-based compensation expense	7,122	5,168
Changes in operating assets and liabilities:		
Other current and long-term assets	(1,226)	72
Accounts payable	(799)	(137)
Payable to Ionis Pharmaceuticals, Inc.	(13,111)	22,086
Accrued compensation	(1,253)	(390)
Deferred rent	4	44
Accrued liabilities	1,136	(2)
Deferred revenue	51,275	—
Net cash provided by (used in) operating activities	6,008	(2,573)
Investing activities:		
Purchases of short-term investments	(61,209)	—
Proceeds from the sale of short-term investments	17,820	6,520
Purchases of property, plant and equipment	—	(45)
Net cash (used in) provided by investing activities	(43,389)	6,475
Financing activities:		
Proceeds from line of credit from Ionis Pharmaceuticals, Inc.	106,000	—
Offering costs paid	(1,031)	(483)
Net cash provided by (used in) financing activities	104,969	(483)
Net increase in cash and cash equivalents	67,588	3,419
Cash and cash equivalents at beginning of period	7,857	29,389
Cash and cash equivalents at end of period	$ 75,445	$ 32,808
Supplemental disclosures of non-cash financing activities:		
Unpaid deferred offering costs	$ 473	$ 379

See accompanying notes.

1. Basis of Presentation and Organization

We prepared the unaudited interim condensed consolidated financial statements for the three and six months ended June 30, 2017 and 2016 on the same basis as the audited financial statements for the year ended December 31, 2016. We included all normal recurring adjustments in the financial statements, which we considered necessary for a fair presentation of our financial position at such dates and our operating results and cash flows for those periods. Results for the interim periods are not necessarily indicative of the results for the entire year. For more complete financial information, these financial statements, and notes thereto, should be read in conjunction with the audited financial statements for the year ended December 31, 2016 included in our final prospectus dated July 13, 2017, filed with the Securities and Exchange Commission, or SEC, on July 14, 2017 pursuant to Rule 424(b)(4) under the Securities Act of 1933, as amended, or the Securities Act.

In the condensed consolidated financial statements we include the accounts of Akcea Therapeutics, Inc. ("we," "our," and "us") and our wholly owned subsidiaries: Akcea Therapeutics UK Ltd., or Akcea UK, (formed in August 2016), Akcea Intl Ltd., or Akcea Intl, (formed in February 2017) and Akcea Therapeutics Canada, Inc., or Akcea Canada (formed in May 2017). We incorporated in Delaware in December 2014. We were organized by Ionis Pharmaceuticals, Inc., or Ionis, to focus on developing and commercializing drugs to treat patients with serious cardiometabolic diseases caused by lipid disorders. As of the date of these financial statements we were wholly owned by Ionis. All intercompany transactions and balances have been eliminated in consolidation. On July 19, 2017, we completed our initial public offering, or IPO. As a result, Ionis is now our majority shareholder.

2. Significant Accounting Policies

Revenue Recognition

We recognize revenue when we have satisfied all contractual obligations and we are reasonably assured of collecting the resulting receivable. We may be entitled to bill our customers and receive payment from our customers in advance of recognizing the revenue. In the instances in which we receive payment from our customers in advance of recognizing revenue, we will include the amounts in deferred revenue on our consolidated balance sheet.

Research and development revenue under collaborative agreements

Arrangements with multiple deliverables

Our strategic collaboration, option and license agreement, or collaboration agreement, with Novartis, which we entered into in January 2017, contains multiple elements, or deliverables, including options to obtain licenses to drugs, research and development services, and manufacturing services. Therefore, we accounted for the collaboration under the multiple deliverables guidance.

Multiple agreements

When we enter into separate agreements at or near the same time with the same partner, we must first evaluate such agreements to determine whether they should be accounted for individually as distinct arrangements or whether the separate agreements are, in substance, a single multiple element arrangement. We evaluate whether the negotiations are conducted jointly as part of a single negotiation, whether the deliverables are interrelated or interdependent, whether fees in one arrangement are tied to performance in another arrangement, and whether elements in one arrangement are essential to another arrangement. Our evaluation involves significant judgment to determine whether a group of agreements might be so closely related that they are, in effect, part of a single arrangement. For example, in the first quarter of 2017, we and Ionis entered into two separate agreements with Novartis at the same time: a collaboration agreement and a stock purchase agreement, or SPA.

We entered into the collaboration agreement with Novartis to develop and commercialize AKCEA-APO(a)-LRx and AKCEA-APOCIII-LRx. Under the collaboration agreement, we received a $75.0 million upfront payment. For each drug, we are responsible for completing a Phase 2 program, conducting an end-of-Phase 2 meeting with the FDA and delivering active pharmaceutical ingredient, or API. Under the collaboration agreement, Novartis has an exclusive option to further develop and commercialize each of AKCEA-APO(a)-LRx and AKCEA-APOCIII-LRx. If Novartis exercises an option for one of these drugs, it will pay us a license fee and will assume all further global development, regulatory and commercialization activities for the licensed drug. We are also eligible to receive a development milestone payment, milestone payments if Novartis achieves pre-specified regulatory milestones, commercial milestones and tiered royalties on net sales from each drug under the collaboration.

Under the SPA, Novartis purchased 1.6 million shares of Ionis' common stock for $100.0 million in the first quarter of 2017 and paid a premium over the weighted average trading price at the time of purchase. Additionally in July 2017, Novartis purchased $50.0 million of our common stock in a separate private placement concurrent with the completion of our IPO. Our IPO is discussed in note 9, *Subsequent Events*.

We evaluated the Novartis agreements to determine whether we should treat the agreements separately or as a single arrangement. We considered that the agreements were negotiated concurrently and in contemplation of one another. Additionally, the same individuals were involved in the negotiations of both agreements. Based on these facts and circumstances, we concluded that we should treat both agreements as a single arrangement, which we refer to as the Novartis collaboration. We evaluated the provisions of the agreements on a combined basis.

Identifying deliverables and units of accounting

We evaluate the deliverables in a collaboration agreement to determine whether they meet the criteria to be accounted for as separate units of accounting or whether they should be combined with other deliverables and accounted for as a single unit of accounting. When the delivered items in an arrangement have "stand-alone value" to the customer, we will account for the deliverables as separate units of accounting. Delivered items have stand-alone value if they are sold separately by any vendor or the customer could resell the delivered items on a stand-alone basis. For example, our Novartis collaboration and SPA have multiple elements. We evaluated the deliverables in the Novartis collaboration when we entered into the agreements and determined that certain deliverables have stand-alone value.

We identified the following four separate units of accounting under the collaboration, each with stand-alone value:

- Development activities for AKCEA-APO(a)-LRx;
- Development activities for AKCEA-APOCIII-LRx;
- API for AKCEA-APO(a)-LRx; and
- API for AKCEA-APOCIII-LRx.

The development activities and the supply of API each have stand-alone value because Novartis or another third party could provide these items without our assistance.

Measurement and allocation of arrangement consideration

Our Novartis collaboration provides for various types of payments to us including upfront payments, milestone payments, licensing fees, royalties on product sales and payments for the purchase of common stock. We first evaluated the total consideration under both the collaboration agreement and SPA and determined how much of the total consideration was attributable to elements that we are delivering under the collaboration.

We determined that our portion of the allocable arrangement consideration for the Novartis collaboration was $108.4 million, comprised of the following:

- $75.0 million from the upfront payment we received;
- $28.4 million for the premium paid by Novartis, which represents the excess of the fair value Ionis received from Novartis' purchase of Ionis' stock at a premium in the first quarter of 2017; and
- $5.0 million for the premium Novartis would have paid to purchase Ionis' stock if we did not complete our IPO within 15 months from the inception of the agreement.

We are recognizing the $75.0 million upfront payment plus the premium paid by Novartis from its purchase of Ionis' stock and the premium associated with Novartis' obligation to purchase Ionis' stock if we did not complete our IPO because we are the party providing the services and API under the collaboration agreement.

We initially allocated the amount of consideration that was fixed or determinable at the time the agreement was entered into and excluded contingent consideration. We allocated the consideration to each unit of accounting based on the relative selling price of each deliverable. We used the following hierarchy of values to estimate the selling price of each deliverable: (i) vendor-specific objective evidence of fair value; (ii) third-party evidence of selling price; and (iii) best estimate of selling price, or BESP. BESP reflects our best estimate of what the selling price would be if we regularly sold the deliverable on a stand-alone basis. We are recognizing the revenue allocated to each unit of accounting as we deliver the related goods or services. If we determine that we should treat certain deliverables as a single unit of accounting, then we will recognize the revenue ratably over our estimated period of performance.

We allocated the consideration based on the relative BESP of each unit of accounting. We estimated the selling price of the development services over the expected period during which we will perform these services. The significant inputs we used to determine the selling price of the development services included:

- The number of internal hours we will spend performing these services;
- The estimated cost of the work we will perform;
- The estimated cost of work that we will contract with third parties to perform; and
- The estimated cost of API we will use.

For purposes of determining BESP of the services we will perform and the API we will deliver under our Novartis collaboration, accounting guidance required us to include a markup for a reasonable profit margin.

Based on the units of accounting under the Novartis collaboration, we allocated the $108.4 million of allocable consideration as follows:

- $64.0 million for development services for AKCEA-APO(a)-LRx;
- $40.1 million for development services for AKCEA-APOCIII-LRx;
- $1.5 million for the delivery of AKCEA-APO(a)-LRx API; and
- $2.8 million for the delivery of AKCEA-APOCIII-LRx API.

Timing of revenue recognition

We recognize revenue as we deliver each item under our Novartis collaboration as we provide services and the related revenue is realizable and earned. We also recognize revenue over time. Our Novartis collaboration agreement includes a development project plan outlining the activities the agreement requires each party to perform during the collaboration. We estimated our period of performance when the agreement was entered into because the agreement did not clearly define such information. We then recognize revenue for development services ratably over such period. We made estimates of our time to complete our obligations under our Novartis collaboration agreement, and in certain instances the timing of satisfying these obligations may change as the development plans for our drugs progress. If our estimates and judgments change over the course of the Novartis collaboration agreement, it may affect the timing and amount of revenue that we will recognize in future periods. Any changes in estimates are recognized on prospective basis.

The following are the periods over which we are recognizing revenue for each of our units of accounting under the Novartis collaboration:

- We are recognizing the amount attributed to the development services for AKCEA-APO(a)-L Rx over the period of time we are performing the services, currently estimated to be through November 2018;
- We are recognizing the amount attributed to the development services for AKCEA-APOCIII-L Rx over the period of time we are performing the services, currently estimated to be through June 2019;
- We will recognize the amount attributed to the AKCEA-APO(a)-LRx API supply when we deliver API to Novartis; and
- We will recognize the amount attributed to the AKCEA-APOCIII-LRx API supply when we deliver API to Novartis.

Milestone payments

Our Novartis collaboration agreement contains contractual milestone payments that relate to the achievement of pre-specified development, regulatory and commercialization events. These three categories of milestone events reflect the three stages of the life-cycle of our drugs, which we describe in more detail in the following paragraphs.

The designation of a development candidate is the first stage in the life-cycle of our drugs. A development candidate is a chemical compound that has demonstrated the necessary safety and efficacy in preclinical animal studies to warrant further study in humans.

During the first step of the development stage, we or our partner study our drugs in Investigational New Drug, or IND,-enabling studies, which are animal studies intended to support an IND application and/or the foreign equivalent. An approved IND allows us or our partners to study our development candidate in humans. If the regulatory agency approves the IND, we or our partners initiate Phase 1 clinical trials in which we typically enroll a small number of healthy volunteers to ensure the development candidate is safe for use in patients. If we or our partners determine that a development candidate is safe based on the Phase 1 data, we or our partners initiate Phase 2 studies that are generally larger scale studies in patients with the primary intent of determining the efficacy of the development candidate.

The final step in the development stage is Phase 3 studies to gather the necessary safety and efficacy data to request marketing authorization from the FDA and/or foreign equivalents. The Phase 3 studies typically involve large numbers of patients and can take up to several years to complete. If the data gathered during the trials demonstrates acceptable safety and efficacy results, we or our partners will submit an application to the FDA and/or its foreign equivalents for marketing authorization. This stage of the drug's life-cycle is the regulatory stage.

If a drug achieves marketing authorization, it moves into the commercialization stage, during which we or our partners will market and sell the drug to patients. Although our partner may ultimately be responsible for marketing and selling the partnered drug, our efforts to develop a drug that is safe, effective and reliable contributes significantly to our partner's ability to successfully sell the drug. The FDA and its foreign equivalents have the authority to impose significant restrictions on an approved drug through the product label and on advertising, promotional and distribution activities. Therefore, our efforts designing and executing the necessary animal and human studies are critical to obtaining claims in the product label from the regulatory agencies that would allow us or our partners to successfully commercialize our drug. Further, the patent protection afforded our drugs as a result of our initial patent applications and related prosecution activities in the United States and foreign jurisdictions are critical to our partner's ability to sell our drugs without competition from generic drugs. The potential sales volume of an approved drug is dependent on several factors including the size of the patient population, market penetration of the drug, and the price charged for the drug.

The milestone events contained in our Novartis collaboration agreement coincide with the progression of our drugs from development, to marketing authorization and then to commercialization. The process of successfully discovering a new development candidate, having it approved and ultimately sold for a profit is highly uncertain. As such, the milestone payments we may earn from our partners involve a significant degree of risk to achieve. Therefore, as a drug progresses through the stages of its life-cycle, the value of the drug generally increases.

Development milestones in our Novartis collaboration agreement or potential future collaborations may include the following types of events:

- Designation of a development candidate. Following the designation of a development candidate, IND-enabling animal studies for a new development candidate generally take 12 to 18 months to complete;
- Initiation of a Phase 1 clinical trial. Generally, Phase 1 clinical trials take one to two years to complete;
- Initiation or completion of a Phase 2 clinical trial. Generally, Phase 2 clinical trials take one to three years to complete; and
- Initiation or completion of a Phase 3 clinical trial. Generally, Phase 3 clinical trials take two to four years to complete.

Regulatory milestones in our Novartis collaboration agreement or potential future collaborations may include the following types of events:

- Filing of regulatory applications for marketing authorization such as a New Drug Application, or NDA, in the United States or a Marketing Authorization Application, or MAA, in Europe. Generally, it takes six to twelve months to prepare and submit regulatory filings.
- Marketing authorization in a major market, such as the United States, Europe or Japan. Generally it takes one to two years after an application is submitted to obtain authorization from the applicable regulatory agency.

Commercialization milestones in our Novartis agreement or potential future collaborations may include the following types of events:

- First commercial sale in a particular market, such as in the United States or Europe.
- Product sales in excess of a pre-specified threshold, such as annual sales exceeding $1 billion. The amount of time to achieve this type of milestone depends on several factors including but not limited to the dollar amount of the threshold, the pricing of the product and the pace at which customers begin using the product.

We will assess whether a substantive milestone exists at the inception of the collaboration agreement. When a substantive milestone is achieved, we will recognize revenue related to the milestone payment immediately. In evaluating if a milestone is substantive we will consider whether:

- Substantive uncertainty exists as to the achievement of the milestone event at the inception of the arrangement;
- The achievement of the milestone involves substantive effort and can only be achieved based in whole or in part on the performance or the occurrence of a specific outcome resulting from its performance;
- The amount of the milestone payment appears reasonable either in relation to the effort expended or to the enhancement of the value of the delivered items;
- There is no future performance required to earn the milestone payment; and
- The consideration is reasonable relative to all deliverables and payment terms in the arrangement.

If any of these conditions are not met, we will not consider the milestone to be substantive and we will defer recognition of the milestone payment and recognize it as revenue over the estimated period of performance, if any. We have determined that all milestones under our Novartis collaboration are substantive milestones.

Option to license

When we have a multiple element arrangement that includes an option to obtain a license, we will evaluate if the option is a deliverable at the inception of the arrangement. We do not consider the option to be a deliverable if we conclude that it is substantive and not priced at a significant and incremental discount. We will consider an option substantive if, at the inception of the arrangement, we are at risk as to whether the collaboration partner will choose to exercise its option to obtain the license. In those circumstances, we do not include the associated license fee in the allocable consideration at the inception of the agreement. Rather, we account for the license fee when our partner exercises its option. Under the Novartis collaboration, we concluded that the option to license is a substantive option. Therefore, we did not include any amounts in the initial allocable consideration at the inception of the collaboration. We will recognize any future exercise of an option to license a drug under our Novartis agreement in full in the period in which the option is exercised.

Refer to note 8, *Strategic Collaboration with Novartis*, where we discuss our Novartis collaboration agreement in more detail.

Cash, Cash Equivalents and Short-Term Investments

We consider all liquid investments with maturities of three months or less when we purchase them to be cash equivalents. Our short-term investments have initial maturities of greater than three months from date of purchase. We classify our short-term investments as available-for-sale and we carry them at fair market value based upon prices for identical or similar items on the last day of the fiscal period. We record unrealized gains and losses as a separate component of comprehensive income (loss) and we include net realized gains and losses in gain (loss) on investments on our consolidated statement of operations. We use the specific identification method to determine the cost of securities sold.

Research and Development Expenses

Our research and development expenses include wages, benefits, facilities, supplies, external services, clinical study and manufacturing costs and other expenses that are directly related to our research and development activities. We expense research and development costs as we incur them.

If we make payments for research and development services prior to the services being rendered, we record those amounts as prepaid assets on our balance sheet and we expense them as the services are provided.

Sublicensing Expenses

We incur sublicense fee expenses under our development, commercialization and license agreement and services agreement with Ionis related to the drugs we have licensed under the agreement. We include our sublicense fee expenses in our research and development expenses on our consolidated results of operations since the applicable drugs are not yet approved for marketing. We recognize sublicense fee expenses in the period they are incurred. For example, in the first quarter of 2017, we incurred $48.4 million of sublicense fee expenses related to our collaboration with Novartis, of which $33.4 million of these expenses were non-cash and were related to the premium Novartis paid and the potential premium Novartis could have paid on Ionis' stock if we did not complete our IPO. Under the Novartis collaboration, we will recognize $108.4 million of revenue over the period of our performance and $48.4 million of sublicensing expense in the first quarter of 2017. The $48.4 million is comprised of the following:

- $15.0 million for the portion of the $75.0 million upfront payment we received upon initiating the Novartis collaboration, which we paid in cash to Ionis;
- $28.4 million for the premium paid by Novartis for its purchase of Ionis' stock in the first quarter of 2017, which is a non-cash expense. We determined the fair value of the premium by calculating the stated premium and applying a discount for lack of marketability because Ionis initially issued unregistered shares to Novartis; and
- $5.0 million for the premium associated with Novartis' obligation to purchase Ionis' stock if we did not complete our IPO, which is a non-cash expense. We determined the fair value of the potential premium at the inception of the collaboration by calculating the value of the future premium based upon the stated premium, adjusting for the probability of us completing an IPO by the 15-month anniversary of the SPA and applying a discount for lack of marketability because Ionis would have issued unregistered shares to Novartis if it purchased Ionis' common stock.

We will pay 50% of all future license fees, milestone payments and royalties we receive to Ionis as a sublicense fee.

Use of Estimates

The preparation of condensed consolidated financial statements in conformity with U.S. GAAP requires our management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Actual results could differ from those estimates.

Basic and Diluted Net Loss Per Share

We issued 28,884,540 shares of Series A convertible preferred stock in December 2015. We used the Series A convertible preferred stock to calculate basic net loss per share because there was no common stock outstanding in any period presented, and the Series A convertible preferred stock represents the lowest subordinated form of outstanding equity. For purposes of calculating diluted net loss per share, we considered the conversion of the Series A convertible preferred stock using its 1:1 conversion ratio and the potential dilutive effect of employee stock options.

Because the Series A convertible preferred stock was the only outstanding form of equity, cumulative accruing dividends on the Series A convertible preferred stock had no effect on net loss available to Ionis, our Series A convertible preferred stock holder. As we incurred a net loss for the three and six months ended June 30, 2017 and 2016, we did not include dilutive common equivalent shares, which consisted of outstanding common stock options in the computation of diluted net loss per share because the effect would have been anti-dilutive.

Accumulated Other Comprehensive Loss

Accumulated other comprehensive loss is comprised of unrealized gains and losses on investments, net of taxes and currency translation adjustments. The following table summarizes changes in accumulated other comprehensive loss for the three and six months ended June 30, 2017 and 2016 (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	2016	2017	2016
Beginning balance accumulated other comprehensive loss	$ (43)	$ (5)	$ (21)	$ (75)
Unrealized losses on securities, net of tax (1)	1	13	(27)	83
Currency translation adjustment	(42)	—	(36)	—
Net current period other comprehensive income	(41)	13	(63)	83
Ending balance accumulated other comprehensive loss	$ (84)	$ 8	$ (84)	$ 8

(1) There was no tax benefit for other comprehensive loss for the three and six months ended June 30, 2017 and 2016.

Translation of Foreign Currency

Akcea UK operates in the United Kingdom and uses the British pound sterling as its functional currency. When we consolidate Akcea UK's financial results, we translate Akcea UK's assets and liabilities using the exchange rate at the balance sheet date and Akcea UK's income and expense items using the average exchange rate for the period. We translate Akcea UK's capital accounts at the historical exchange rate in effect at the date of the transaction. We record adjustments resulting from the translation of Akcea UK's financial statements as a separate component of stockholders' equity (deficit) in accumulated other comprehensive income. Our other foreign subsidiaries translation of foreign currency is immaterial to our financial results.

Segment Information

We operate as a single segment because our chief decision maker reviews operating results on an aggregate basis and manages our operations as a single operating segment.

Stock-Based Compensation Expense

We measure stock-based compensation expense for equity-classified stock option awards based on the estimated fair value of the award on the date of grant. We recognize the value of the portion of the award that we ultimately expect to vest as stock-based compensation expense over the requisite service period in our statements of operations. We reduce stock-based compensation expense for estimated forfeitures at the time of grant and revise the expense in subsequent periods if actual forfeitures differ from those estimates.

We value our stock option awards using the Black-Scholes model. The determination of the grant date fair value of options using an option pricing model is affected principally by our estimated common stock fair value and requires us to make a number of other assumptions, including: the expected life of the option, the volatility of the underlying stock, the risk-free interest rate and expected dividends.

Prior to December 2015, Ionis granted our employees options to purchase shares of Ionis' common stock, or Ionis options. In December 2015, we granted our employees holding Ionis options additional options to purchase shares of our common stock, or Akcea options. Subject to service based vesting requirements, the Ionis options only become exercisable if (1) we are not acquired or if we do not complete a qualified financing transaction, such as an IPO, by June 30, 2017 and (2) the employee forfeits his or her Akcea equity. Upon the consummation of any such transaction (even if occurring after June 30, 2017), our employees would forfeit their rights to the Ionis options that they hold such that under no circumstances would an employee be able to exercise both Ionis options and Akcea options. As such, in July 2017 when we completed our IPO, the Ionis options our employees were holding were terminated.

We determined the stock-based compensation expense for the Ionis options at the date of grant and recognized compensation expense over the vesting period of the Ionis options. In December 2015, we accounted for the issuance of the Akcea options as a modification to the original grant of the Ionis options because the grant of the Ionis options and Akcea options essentially represented a single stock award as the exercisability provisions of the Ionis options and Akcea options grants were interrelated and mutually exclusive. The total compensation expense measured on the modification date was the sum of the grant date fair value of the Ionis options plus any incremental compensation cost resulting from the grant of the Akcea options.

In 2016, we began concurrently granting Ionis options and Akcea options to our employees. Because the exercisability provisions of the awards are interrelated and mutually exclusive as described above, the fair values of the Ionis options and the Akcea options were determined on the date of grant and the option with the greater fair value is recognized over the vesting period of the awards. Our board of directors only receive grants under the Akcea option plan. Following our IPO, we no longer grant Ionis options to our employees.

For the six months ended June 30, 2017 and 2016, we used the following weighted-average assumptions in our Black-Scholes calculations for stock option grants under our 2015 Equity Incentive Plan:

Employee Stock Options:

	Six Months Ended June 30,	
	2017	2016
Risk-free interest rate	1.9%	1.6%
Dividend yield	0.0%	0.0%
Volatility	79.4%	69.3%
Expected life	6.08 years	6.08 years
Fair value of common stock	$ 12.12	$ 6.48

Board of Director Stock Options:

	Six Months Ended June 30, 2017
Risk-free interest rate	1.9%
Dividend yield	0.0%
Volatility	79.4%
Expected life	6.25 years
Fair value of common stock	$ 12.12

We did not grant any options to our board of directors during the six months ended June 30, 2016.

The fair value of stock options granted under our 2015 Equity Incentive Plan is based on the fair value of our common stock on the date of grant.

For the six months ended June 30, 2017 and 2016, we used the following weighted-average assumptions in our Black-Scholes calculations for stock option grants under the Ionis 2011 Equity Incentive Plan:

Employee Stock Options:

	Six Months Ended June 30,	
	2017	2016
Risk-free interest rate	1.8%	1.5%
Dividend yield	0.0%	0.0%
Volatility	65.8%	59.1%
Expected life	4.5 years	4.5 years

The fair value of stock options granted under the Ionis 2011 Equity Incentive Plan is based on the fair value of Ionis' common stock on the date of grant.

The following table summarizes stock-based compensation expense for the three months ended June 30, 2017 and 2016 (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	2016	2017	2016
Research and development expenses	$ 1,919	$ 1,311	$ 3,520	$ 2,147
General and administrative expenses	2,023	667	3,602	3,021
Total	$ 3,942	$ 1,978	$ 7,122	$ 5,168

As of June 30, 2017, total unrecognized estimated non-cash stock-based compensation expense related to non-vested stock options was $23.0 million. We will adjust total unrecognized compensation cost for future forfeitures. We expect to recognize the cost of non-cash stock-based compensation expense related to non-vested stock options over a weighted average amortization period of 1.5 years.

Income Taxes

Prior to the completion of our IPO, we were included in Ionis' consolidated U.S. federal income tax return filing. For these consolidated financial statements, we are using the separate return method, which determines income taxes as if we were a separate taxpayer from Ionis. As a result of our IPO, beginning in the third quarter of 2017, we will no longer file a consolidated federal tax return with Ionis. We have not determined the amount of tax attributes, including net operating losses and tax credit carryovers that will transfer over to us upon deconsolidation from Ionis.

Impact of Recently Issued Accounting Standards

In May 2014, the Financial Accounting Standards Board, or FASB, issued accounting guidance on the recognition of revenue from customers. Under this guidance, an entity will recognize revenue when it transfers promised goods or services to customers in an amount that reflects what the entity expects to receive in exchange for the goods or services. This new guidance also requires more detailed disclosures to enable users of the financial statements to understand the nature, amount, timing and uncertainty of revenue and cash flows arising from contracts with customers. The guidance as originally issued is effective for annual and interim periods, beginning after December 15, 2016. In July 2015, the FASB issued updated accounting guidance to allow for an optional one-year deferral from the original effective date. As a result, we will adopt this guidance beginning on January 1, 2018. Prior to 2017, we had not generated revenue. In January 2017, we entered into a strategic collaboration agreement with Novartis and began recognizing revenue. We will adopt this guidance under the full retrospective approach, meaning we will apply the guidance to all periods presented. Given that we recently entered into the Novartis collaboration agreement, we are currently determining the effects the adoption will have on our consolidated financial statements and disclosures.

In January 2016, the FASB issued amended accounting guidance related to the recognition, measurement, presentation, and disclosure of certain financial instruments. The amended guidance requires us to measure and record equity investments at fair value, except those accounted for under the equity method of accounting that have a readily determinable fair value, and for us to recognize the changes in fair value in our net income (loss), instead of recognizing unrealized gains and losses through accumulated other comprehensive income, as we currently do under the existing guidance. The amended guidance also changes several disclosure requirements for financial instruments, including the methods and significant assumptions we use to estimate fair value. The guidance is effective for annual and interim periods, beginning after December 15, 2017. We will adopt this guidance on January 1, 2018 and we will make any adjustments to beginning balances through a cumulative-effect adjustment to accumulated deficit on that date. We are currently determining the effects the adoption will have on our consolidated financial statements and disclosures.

In February 2016, the FASB issued amended accounting guidance related to lease accounting, which requires us to record all leases with a term longer than one year on our balance sheet. When we record leases on our balance sheet under the new guidance, we will record a liability with a value equal to the present value of payments we will make over the life of the lease and an asset representing the underlying leased asset. The new accounting guidance requires us to determine if any lease we have is an operating or financing lease, similar to current accounting guidance. We will record expense for an operating type lease on a straight-line basis as an operating expense and we will record expense for a finance type lease as interest expense. The new lease standard is effective for annual and interim periods beginning after December 15, 2018, with early adoption permitted. We must adopt the new standard on a modified retrospective basis, which requires us to reflect any leases we have on our consolidated balance sheet for the earliest comparative period presented. We are currently assessing the timing of adoption as well as the effects it will have on our consolidated financial statements and disclosures.

In March 2016, the FASB issued amended guidance to simplify certain aspects of share-based payment accounting. Under the amended guidance, we will recognize excess tax benefits and tax deficiencies as income tax expense or benefit in our consolidated statement of operations on a prospective basis. As we have a valuation allowance, this change will impact our net operating loss carryforward and the valuation allowance disclosures. Additionally, we will classify excess tax benefits as an operating activity and classify amounts we withhold in shares for the payment of employee taxes as a financing activity on the consolidated statement of cash flows for each period presented. Lastly, the amended guidance allows us to account for forfeitures when they occur or continue to estimate them. We will continue to estimate our forfeitures. The amended share-based payment standard is effective for annual and interim periods beginning after December 15, 2016, with early adoption permitted in any interim or annual period. We adopted this guidance on January 1, 2017. The amended guidance did not impact our financial results.

In June 2016, the FASB issued guidance that changes the measurement of credit losses for most financial assets and certain other instruments. If we have credit losses, this updated guidance requires us to record allowances for these instruments under a new expected credit loss model. This model requires us to estimate the expected credit loss of an instrument over its lifetime, which represents the portion of the amortized cost basis we do not expect to collect. This change will result in us remeasuring our allowance in each reporting period we have credit losses. The new standard is effective for annual and interim periods beginning after December 15, 2019. Early adoption is permitted for periods beginning after December 15, 2018. When we adopt the new standard, we will make any adjustments to beginning balances through a cumulative-effect adjustment to accumulated deficit on that date. We are currently assessing the timing of adoption as well as the effects it will have on our consolidated financial statements and disclosures.

In May 2017, the FASB issued clarifying guidance related to the accounting for modifications of share-based payment awards. The new guidance is meant to clarify when modification accounting is required. We early adopted this guidance in these financial statements for the quarter ended June 30, 2017 and it did not have an effect on our consolidated financial statements and disclosures.

3. Investments

As of June 30, 2017, we primarily invested our excess cash in debt instruments of the U.S. Treasury, financial institutions, corporations, and U.S. government agencies with strong credit ratings and an investment grade rating at or above A-1, P-1 or F-1 by Moody's, Standard & Poor's or Fitch, respectively. We have established guidelines relative to diversification and maturities that maintain safety and liquidity. We periodically review and modify these guidelines to maximize trends in yields and interest rates without compromising safety and liquidity.

As of June 30, 2017, all of the securities held by us had a contractual maturity of one year or less and all of our available-for-sale securities were available to us for use in our current operations and are classified as current assets.

As of December 31, 2016, we only invested in money market funds.

The following is a summary of our investments at June 30, 2017 (in thousands):

	Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Available-for-sale securities (1):				
Corporate debt securities	$ 40,250	$ —	$ (25)	$ 40,225
Other municipal debt securities	3,000	—	(2)	2,998
Total available-for-sale securities	$ 43,250	$ —	$ (27)	$ 43,223

(1) Our available-for-sale securities are held at amortized cost.

Investments we consider to be temporarily impaired at June 30, 2017 were as follows (in thousands):

	Number of Investments	Less than 12 Months of Temporary Impairment: Estimated Fair Value	Less than 12 Months of Temporary Impairment: Unrealized Losses	More than 12 Months of Temporary Impairment: Estimated Fair Value	More than 12 Months of Temporary Impairment: Unrealized Losses	Total Temporary Impairment: Estimated Fair Value	Total Temporary Impairment: Unrealized Losses
Corporate debt securities	17	$ 31,437	$ (25)	$ —	$ —	$ 31,437	$ (25)
Other municipal debt securities	1	2,998	(2)	—	—	2,998	(2)
Total temporarily impaired securities	18	$ 34,435	$ (27)	$ —	$ —	$ 34,435	$ (27)

We believe that the decline in value of these securities is temporary and are primarily related to the change in market interest rates since purchase. We believe it is more likely than not that we will be able to hold our debt securities to maturity. Therefore, we anticipate a full recovery of our debt securities' amortized cost basis at maturity.

4. Fair Value Measurements

We use a three-tier fair value hierarchy to prioritize the inputs used in our fair value measurements. These tiers include: Level 1, defined as observable inputs such as quoted prices in active markets for identical assets, which includes our money market funds and treasury securities classified as available-for-sale securities; Level 2, defined as inputs other than quoted prices in active markets that are either directly or indirectly observable, which includes our fixed income securities and commercial paper classified as available-for-sale securities; and Level 3, defined as unobservable inputs in which little or no market data exists, therefore requiring us to develop our own assumptions. We have not held any Level 3 investments. Our securities have been classified as Level 1 or Level 2. We obtain the fair value of our Level 2 investments from our custodian bank and from a professional pricing service. We validate the fair value of our Level 2 investments by understanding the pricing model used by the custodian banks or professional pricing service provider and comparing that fair value to the fair value based on observable market prices. During six months ended June 30, 2017, there were no transfers between our Level 1 and Level 2 investments. We recognize transfers between levels of the fair value hierarchy on the date of the event or change in circumstances that caused the transfer. We did not have any Level 3 investments or liabilities at June 30, 2017 and at December 31, 2016.

At December 31, 2016, we held $7.1 million of money market fund investments which are Level 1 investments and are considered cash equivalents. The following tables present the major security types we held at June 30, 2017, that are regularly measured and carried at fair value. The table segregates each security by the level within the fair value hierarchy of the valuation techniques we utilized to determine the respective securities' fair value (in thousands):

	At June 30, 2017	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)
Cash equivalents (1)	$ 69,107	$ 69,107	$ —
Corporate debt securities (2)	40,225	—	40,225
Other municipal debt securities (2)	2,998	—	2,998
Total	$ 112,330	$ 69,107	$ 43,223

(1) Included in cash and cash equivalents on our condensed consolidated balance sheets.

(2) Included in short-term investments on our condensed consolidated balance sheets.

5. Development, Commercialization and License Agreement and Services Agreement with Ionis

We entered into a development, commercialization and license agreement and a services agreement in December 2015 with Ionis. The following section summarizes these related party agreements with Ionis.

Development, Commercialization and License Agreement

Our development, commercialization and license agreement, or the license agreement, with Ionis granted exclusive rights to us to develop and commercialize volanesorsen, AKCEA-APO(a)-LRx, AKCEA-APOCIII-LRx, and AKCEA-ANGPTL3-LRx, which are collectively referred to as the Lipid Drugs. As a part of the grant to us from Ionis, Ionis has granted an exclusive license to certain patents to develop and commercialize products containing the Lipid Drugs. Ionis also granted us a non-exclusive license to the Ionis antisense platform technology for us to develop and commercialize products containing the Lipid Drugs. Ionis also granted us non-exclusive rights under its manufacturing technology to manufacture the Lipid Drugs in our own facility, or at a contract manufacturer. As a part of this agreement both companies agreed not to work with any other parties to develop or commercialize other drugs that are designed to inhibit any of the Lipid Drug targets so long as we are developing or commercializing the Lipid Drugs.

We and Ionis share development responsibilities for the Lipid Drugs. We pay Ionis for the research and development expenses it incurs on our behalf, which include both external and internal expenses. External research and development expenses include costs for contract research organizations, or CROs, costs to conduct nonclinical and clinical studies on our drugs, costs to acquire and evaluate clinical study data such as investigator grants, patient screening fees and laboratory work, and fees paid to consultants. Internal research and development expenses include costs for the work that Ionis' research and development employees perform for us. Ionis charges us a full-time equivalent rate that covers personnel-related expenses, including salaries and benefits, plus an allocation of facility-related expenses, including rent, utilities, insurance and property taxes, for those development employees who work either directly or indirectly on the development of our drugs. We also pay Ionis for the active pharmaceutical ingredient, or API, and drug product we use in our nonclinical and clinical studies for all of our drugs. Ionis manufactures the API for us and charges us a price per gram consistent with the price Ionis charges its pharmaceutical partners, which includes the cost for direct materials, direct labor and overhead required to manufacture the API. If we need the API filled in vials for our clinical studies, Ionis will contract with a third party to perform this work and Ionis will charge us for the resulting cost.

As we commercialize each of the Lipid Drugs, we will pay Ionis royalties from the mid-teens to the mid-twenty percent range on sales related to the Lipid Drugs that we sell. If we sell a Lipid Drug for a Rare Disease Indication (defined in the agreement as less than 500,000 patients worldwide or an indication that required a Phase 3 program of less than 1,000 patients and less than two years of treatment), we will pay a higher royalty rate to Ionis than if we sell a Lipid Drug for a Broad Disease Patient Population (defined in the agreement as more than 500,000 patients worldwide or an indication that required a Phase 3 program of 1,000 or more patients and two or more years of treatment). Other than with respect to the drugs licensed to Novartis under the collaboration agreement, if our annual sales reach $500.0 million, $1.0 billion and $2.0 billion, we will be obligated to pay Ionis sales milestones in the amount of $50.0 million for each sales milestone reached by each Lipid Drug. If and when triggered, we will pay Ionis each of these sales milestones over the subsequent 12 quarters in equal payments.

We may terminate this agreement if Ionis is in material breach of the agreement. Ionis may terminate this agreement if we are in material breach of the agreement. In each circumstance the party that is in breach will have an opportunity to cure the breach prior to the other party terminating this agreement.

In the first quarter of 2017, we entered into letter agreements with Ionis to reflect the agreed upon payment terms with respect to the upfront option payment that we received from Novartis and to allocate the premium that Novartis paid for Ionis' common stock in connection with our strategic collaboration with Novartis. For additional detail regarding our strategic collaboration with Novartis see note 8, *Strategic Collaboration with Novartis.*

Services Agreement

Under the services agreement, Ionis provides us certain services, including, without limitation, general and administrative support services and development support services. Ionis has allocated a certain percentage of personnel to perform the services that it provides to us based on its good faith estimate of the required services. We pay Ionis for these allocated costs, which reflect the Ionis full-time equivalent, or FTE, rate for the applicable personnel, plus out-of-pocket expenses such as occupancy costs associated with the FTEs allocated to providing us these services. We do not pay a mark-up or profit on the external or internal expenses Ionis bills to us. Ionis invoices us quarterly for all amounts due under the services agreement and payments are due within 30 days of the receipt of an invoice.

In addition, as long as Ionis continues to consolidate our financials, we will comply with Ionis' policies and procedures and internal controls. As long as we are consolidated into Ionis' financial statements under U.S. GAAP, we will continue to obtain the following services from Ionis:

- investor relations services,
- human resources and personnel services,
- risk management and insurance services,
- tax related services,
- corporate record keeping services,
- financial and accounting services,
- credit services, and
- COO/CFO/CBO oversight.

However, if we wanted to provide for our own human resources and personnel services, and doing so would not negatively impact Ionis' internal controls and procedures for financial reporting, we can negotiate in good faith with Ionis for a reduced scope of services related to human resources and personnel services. When Ionis determines it should no longer consolidate our financials, we may mutually agree with Ionis in writing to extend the term in six-month increments.

We can establish our own benefits programs or can continue to use Ionis' benefits, however, we must provide Ionis a minimum advance notice to opt-out of using Ionis' benefits.

As of June 30, 2017 and December 31, 2016, we owed Ionis $11.2 million and $24.4 million, respectively.

The following table summarizes the amounts included in our operating expenses that were generated by transactions with Ionis for the following periods (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	2016	2017	2016
Services performed by Ionis	$ 2,998	$ 2,059	$ 5,955	$ 4,112
Active pharmaceutical ingredient manufactured by Ionis	2,930	—	6,013	—
Sublicensing expenses	—	—	48,394	—
Out-of-pocket expenses paid by Ionis	5,316	8,123	17,189	17,974
Total expenses generated by transactions with Ionis	11,244	10,182	77,551	22,086
Payable balance to Ionis at the beginning of the period	15,000	21,102	$ 24,355	9,198
Less: total amounts paid to Ionis during the period	(15,000)	—	(57,268)	—
Less: non-cash sublicensing expenses	—	—	(33,394)	—
Total amount payable to Ionis at period end	$ 11,244	$ 31,284	$ 11,244	$ 31,284

6. Line of Credit Agreement with Ionis

In January 2017, we entered into a line of credit agreement with Ionis for up to $150.0 million. We had $106.0 million outstanding as of June 30, 2017. We used a portion of the $106.0 million to pay our intercompany expenses. The amounts we borrowed under the line of credit bore interest at an annual interest rate of 4%, compounded monthly. At June 30, 2017, the outstanding balance on the line of credit with Ionis, including principal and interest, was $107.5 million. For the three and six months ended June 30, 2017, interest expense was $1.0 million and $1.5 million.

The outstanding principal and accrued interest under our line of credit converted into 13,438,339 shares of our common stock in connection with the closing of our IPO.

Additionally, we no longer have access to this line of credit following the closing of our IPO. Our IPO is discussed in note 9, *Subsequent Events*.

7. Stockholders' Equity (Deficit)

Series A Convertible Preferred Stock

In December 2015, we issued and sold to Ionis an aggregate of 28,884,540 shares of Series A convertible preferred stock for a total purchase price of $100.0 million plus the grant of the rights and licenses we received under the development, commercialization and license agreement with Ionis. The $100.0 million of proceeds we received was recorded in Series A convertible preferred stock on our consolidated balance sheet. We had 28,884,540 shares of Series A convertible preferred stock authorized, issued and outstanding as of June 30, 2017 and December 31, 2016, of which all was held by Ionis.

Conversion

Shares of our Series A convertible preferred stock were convertible 1:1 into common stock, subject to certain adjustments for reorganizations, reclassifications, stock splits, stock dividends and dilutive issuances. All shares of Series A convertible preferred stock automatically converted into common stock upon completion of the IPO in July 2017. Our IPO is discussed in note 9, *Subsequent Events*.

Common Stock

At June 30, 2017 and December 31, 2016, we had 100,000,000 shares of common stock authorized, of which none was issued or outstanding.

In May 2017, our board of directors approved an amendment to our certificate of incorporation to (1) effect a reverse stock split on outstanding shares of our common stock and preferred stock on a one-for-2.555 basis, (2) decrease the authorized shares of our preferred stock to 40,000,000 and (3) modify the threshold for automatic conversion of our preferred stock into shares of our common stock in connection with an IPO to eliminate the price per share threshold and only require that we raise at least $50.0 million in gross proceeds (collectively, the "Charter Amendment"). The par values of the common stock and preferred stock were not adjusted as a result of the reverse stock split. The amendment to our certificate of incorporation was approved by our stockholder and became effective upon the filing with the State of Delaware in June 2017. All issued and outstanding common stock and preferred stock and related share and per share amounts contained in these condensed consolidated financial statements have been retroactively adjusted to reflect the reverse stock split for all periods presented.

Stock Plans

2015 Equity Incentive Plan

In December 2015, our board of directors and stockholders adopted and approved our 2015 Equity Incentive Plan, or the 2015 Plan. In May 2017 and June 2017, our board of directors and stockholder, respectively, approved an amendment to our 2015 Equity Incentive Plan in order to, among other things, increase the number of shares of common stock reserved for issuance thereunder to 8,500,000 shares of common stock in conjunction with the IPO.

As of June 30, 2017 and after giving effect to the IPO, the aggregate number of shares of common stock that may be issued pursuant to stock awards under the 2015 Plan was 8,500,000 shares. The 2015 Plan also provides for the grant of nonstatutory stock options, or NSOs, incentive stock options, or ISOs, stock appreciation rights, restricted stock awards, and restricted stock unit awards. At June 30, 2017, options with respect to a total of 6,742,246 shares of common stock were outstanding, of which 2,278,211 were exercisable, and 1,757,754 shares were available for future grant under the 2015 Plan, after giving effect to the IPO.

2017 Employee Stock Purchase Plan

In May 2017 and June 2017, our board of directors and stockholder, respectively, approved our 2017 Employee Stock Purchase Plan, or 2017 ESPP, which became effective upon the completion of our IPO, and the reservation for issuance thereunder of 500,000 shares of common stock. As of June 30, 2017, there were no shares outstanding under our 2017 ESPP.

8. Strategic Collaboration with Novartis

In January 2017, we initiated a strategic collaboration with Novartis for the development and commercialization of AKCEA-APO(a)-LRx and AKCEA-APOCIII-LRx. Under the Novartis collaboration, Novartis has an exclusive option to further develop and commercialize these drugs. We are responsible for completing a Phase 2 program, conducting an end-of-Phase 2 meeting with the FDA and providing API for each drug. If Novartis exercises an option for one of these drugs, Novartis will be responsible, at its expense, to use commercially reasonable efforts to further develop and commercialize that drug. We received a $75.0 million upfront payment in the first quarter of 2017, of which we retained $60.0 million and we paid Ionis $15.0 million as a sublicense fee under our license agreement with Ionis.

If Novartis exercises its option for a drug, Novartis will pay us a license fee equal to $150.0 million for each drug licensed by Novartis. In addition, for AKCEA-APO(a)-LRx, we are eligible to receive up to $600.0 million in substantive milestone payments, including $25.0 million for the achievement of a development milestone, up to $290.0 million for the achievement of regulatory milestones and up to $285.0 million for the achievement of commercialization milestones. In addition, for AKCEA-APOCIII-LRx, we are eligible to receive up to $530.0 million in substantive milestone payments, including $25.0 million for the achievement of a development milestone, up to $240.0 million for the achievement of regulatory milestones and up to $265.0 million for the achievement of commercialization milestones. We plan to co-commercialize any licensed drug commercialized by Novartis in selected markets, under terms and conditions that we plan to negotiate with Novartis in the future. We will earn the next milestone payment of $25.0 million under this collaboration if Novartis advances the Phase 3 study for either drug. We are also eligible to receive tiered royalties in the mid-teens to low twenty percent range on net sales of AKCEA-APO(a)-LRx and AKCEA-APOCIII-LRx. Novartis will reduce these royalties upon the expiration of certain patents or if a generic competitor negatively impacts the product in a specific country. We will pay 50% of these license fees, milestone payments and royalties to Ionis as a sublicense fee.

The agreement with Novartis will continue until the earlier of the date that all of Novartis' options to obtain the exclusive licenses under the agreement expire unexercised or, if Novartis exercises its options, until the expiration of all payment obligations under the agreement. In addition, the agreement as a whole or with respect to any drug under the agreement, may terminate early under the following situations:

- Novartis may terminate the agreement as a whole or with respect to any drug at any time by providing written notice to us;
- Either us or Novartis may terminate the agreement with respect to any drug by providing written notice to the other party in good faith that we or Novartis have determined that the continued development or commercialization of the drug presents safety concerns that pose an unacceptable risk or threat of harm in humans or would violate any applicable law, ethical principles, or principles of scientific integrity;
- Either we or Novartis may terminate the agreement for a drug by providing written notice to the other party upon the other party's uncured failure to perform a material obligation related to the drug under the agreement, or the entire agreement if the other party becomes insolvent; and
- We may terminate the agreement if Novartis disputes or assists a third party to dispute the validity of any of our or Ionis' patents.

Additionally, in January 2017, we and Ionis entered into a SPA with Novartis. Under the SPA, in July 2017, as part of our IPO, Novartis purchased $50.0 million of our common stock in a separate private placement concurrent with the completion of our IPO at a price per share equal to the IPO price. Our IPO is discussed in note 9, *Subsequent Events*.

During the three and six months ended June 30, 2017, we earned revenue of $14.1 million and $23.7 million, respectively from our relationship with Novartis, representing 100% of our revenue for each period. Our consolidated balance sheet at June 30, 2017 included deferred revenue of $84.7 million related to our relationship with Novartis.

9. Subsequent Events

On July 19, 2017, we completed our IPO. Total net proceeds were $182.4 million, including the following:

- $132.4 million from the sale of 17,968,750 shares of our common stock in our IPO; and
- $50.0 million from the purchase of 6,250,000 shares by Novartis in a concurrent private placement.

In addition, both of the following occurred in connection with the completion of our IPO on July 19, 2017:

- the conversion of all outstanding shares of Series A convertible preferred stock into 28,884,540 shares of our common stock; and
- the conversion of $106.0 million of outstanding principal plus accrued interest from the line of credit into 13,438,339 shares of common stock.

The following table summarizes certain actual balance sheet data and pro forma balance sheet data to reflect the activities related to our IPO noted above and Novartis' concurrent private placement, as of June 30, 2017 (in thousands):

	June 30, 2017	Pro Forma June 30, 2017
Cash and cash equivalents and short-term investments	$ 118,668	$ 302,382
Other current assets	3,939	2,052
Accounts payable and accrued expenses	3,608	2,998
Line of credit with Ionis Pharmaceuticals, Inc.	107,507	—
Convertible preferred stock	100,000	—
Common stock	—	67
Additional paid-in capital	64,059	453,936
Total stockholders' equity (deficit)	(82,983)	206,961

ITEM 2 MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

In this Report on Form 10-Q, unless the context requires otherwise, "Akcea," "Company," "we," "our," and "us," means Akcea Therapeutics, Inc and our subsidiaries.

Forward-Looking Statements

In addition to historical information contained in this Report on Form 10-Q, this Report includes forward-looking statements regarding our financial position, outlook and our business, and the therapeutic and commercial potential of volanesorsen and our other products in development. Any statement describing our goals, expectations, financial or other projections, intentions or beliefs, is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs. Our forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause our results to differ materially from those expressed or implied by such forward-looking statements. Although our forward-looking statements reflect the good faith judgment of our management, these statements are based only on facts and factors currently known by us. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning our programs are described in additional detail in our final prospectus dated July 13, 2017, filed with the SEC on July 14, 2017 pursuant to Rule 424(b)(4) under the Securities Act, in connection with our IPO, and those identified within this Item in the section entitled "Risk Factors" beginning on page 24 of this Report.

The following discussion and analysis should be read in conjunction with our financial statements and accompanying notes included in this Quarterly Report on Form 10-Q and the financial statements and accompanying notes thereto for the fiscal year ended December 31, 2016 and the related Management's Discussion and Analysis of Financial Condition and Results of Operations, which are contained in our final prospectus dated July 13, 2017, filed with the SEC on July 14, 2017 pursuant to Rule 424(b)(4) under the Securities Act, in connection with our IPO.

Overview

We are a late-stage biopharmaceutical company focused on developing and commercializing drugs to treat patients with serious cardiometabolic diseases caused by lipid disorders. Our goal is to become the premier company offering treatments for inadequately treated lipid disorders. We are advancing a mature pipeline of four novel drugs with the potential to treat multiple diseases. Our drugs, volanesorsen, AKCEA-APO(a)-L_{Rx}, AKCEA-ANGPTL3-L_{Rx} and AKCEA-APOCIII-L_{Rx}, are all based on antisense technology developed by Ionis Pharmaceuticals, Inc., or Ionis. Our most advanced drug, volanesorsen, has completed a Phase 3 clinical program for the treatment of familial chylomicronemia syndrome, or FCS, and is currently in Phase 3 clinical development for the treatment of familial partial lipodystrophy, or FPL. FCS and FPL are both severe, rare, genetically defined lipid disorders characterized by extremely elevated levels of triglycerides. Both diseases have life-threatening consequences and the lives of patients with these diseases are impacted daily by the associated symptoms. In our clinical program, we have observed consistent and substantial (>70%) decreases in triglycerides and improvements in other manifestations of FCS, including pancreatitis attacks and abdominal pain. We believe the safety and efficacy data from the volanesorsen program demonstrate a favorable risk-benefit profile for patients with FCS. In July 2017 we, working closely with Ionis, filed for marketing authorization for volanesorsen to treat patients with FCS in the EU. We and Ionis plan to file for marketing authorization in the U.S. and Canada in September 2017.

We are continuing to assemble the infrastructure to commercialize our drugs globally with a focus on lipid specialists as the primary call point. A key element of our commercial strategy is to provide the specialized, patient-centric support required to successfully address rare disease patient populations. We believe our focus on treating patients with inadequately addressed lipid disorders will allow us to partner efficiently and effectively with the specialized medical community that supports these patients.

To maximize the commercial potential of two of the drugs in our pipeline, we initiated a strategic collaboration with Novartis Pharma AG, or Novartis, for the development and commercialization of AKCEA-APO(a)-L_{Rx} and AKCEA-APOCIII-L_{Rx}. We believe Novartis brings significant resources and expertise to the collaboration that can accelerate our ability to deliver these potential therapies to the large populations of patients who have high cardiovascular risk due to inadequately treated lipid disorders. After we complete Phase 2 development of each of AKCEA-APO(a)-L_{Rx}. and AKCEA-APOCIII-L_{Rx}, if, on a drug by drug basis, Novartis exercises its option to license a drug, Novartis plans to conduct and pay for a Phase 3 cardiovascular outcome study in high-risk patients and, if approved, to commercialize such drug worldwide. We plan to co-commercialize any approved drugs resulting from this collaboration with Novartis in selected markets, under terms and conditions that we plan to negotiate with Novartis in the future, through the specialized sales force we are building to commercialize volanesorsen.

Our strategic collaboration with Novartis has a potential aggregate transaction value of over $1.0 billion, plus royalties, which we will generally share equally with Ionis. The calculation of potential aggregate transaction value assumes that Novartis licenses, successfully develops and achieves regulatory approval for both AKCEA-APO(a)-L_{Rx} and AKCEA-APOCIII-L_{Rx} in the United States, Europe and Japan, and that Novartis achieves pre-specified sales targets with respect to both drugs. We received $75.0 million in an upfront option payment, of which we retained $60.0 million and paid $15.0 million as a sublicense fee under our license agreement with Ionis. If Novartis exercises its option for a drug, Novartis will pay us a license fee equal to $150.0 million for each drug licensed by Novartis. In addition, for AKCEA-APO(a)-L_{Rx} we are eligible to receive up to $600.0 million in milestone payments, including $25.0 million for the achievement of a development milestone, up to $290.0 million for the achievement of regulatory milestones and up to $285.0 million for the achievement of commercialization milestones. In addition, for AKCEA-APOCIII-L_{Rx} we are eligible to receive up to $530.0 million in milestone payments, including $25.0 million for the achievement of a development milestone, up to $240.0 million for the achievement of regulatory milestones and up to $265.0 million for the achievement of commercialization milestones. Further, we are eligible to receive tiered royalties in the mid-teens to low twenty percent range on net sales of each drug. As a sublicense fee, we will pay to Ionis 50% of the license fees, milestone payments and royalties we receive from Novartis. See note 8, *Strategic Collaboration with Novartis,* to our condensed consolidated financial statements for additional information.

Through 2016, we did not generate revenue and we have incurred net losses in each period since inception. In January 2017, we initiated a strategic collaboration with Novartis and began recognizing revenue under this collaboration. Our revenue for the first half of 2017 was $23.7 million. Our net losses have resulted from costs incurred in developing volanesorsen and the other drugs in our pipeline, preparing to commercialize volanesorsen and general and administrative activities associated with our operations. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future as we continue to develop volanesorsen and our other drugs, and seek regulatory approval for and prepare to commercialize volanesorsen. We expect to incur significant expenses to continue to build the infrastructure to support volanesorsen's commercialization, including manufacturing, marketing, sales and distribution functions. Further, we expect to incur additional costs associated with operating as a public company and in building our internal resources to become less reliant on Ionis.

We have funded our operating activities through a $100.0 million cash contribution that we received from Ionis in 2015, $75.0 million from initiating our collaboration with Novartis that we received in the first quarter of 2017 and $106.0 million in drawdowns under our line of credit with Ionis that we received in the first and second quarters of 2017. In July 2017 we completed our IPO and raised $182.4 million in net proceeds from the IPO including the $50 million Novartis concurrent private placement. We plan to further advance our drugs and commercialization efforts with our cash on hand and these proceeds. As of June 30, 2017, we had cash, cash equivalents and short-term investments of $118.7 million, which does not include the $182.4 million we received from our IPO and concurrent private placement from Novartis.

We believe that the net proceeds from our IPO and the concurrent private placement, together with our existing cash, cash equivalents and short-term investments, will be sufficient to fund our operations for at least the next 12 months. However, we will need to raise additional capital in the future to continue developing the drugs in our pipeline and to commercialize any approved drug, including volanesorsen. We may seek to obtain additional financing in the future through the issuance of our common stock, through other equity or debt financings or through collaborations or partnerships with other companies. We may not be able to raise additional capital on terms acceptable to us, or at all, and any failure to raise capital as and when needed could compromise our ability to execute on our business plan.

Our Relationship with Ionis

Prior to January 2015, the drugs we licensed from Ionis were part of Ionis' broad pipeline of antisense drugs. Ionis' employees performed all of the development, regulatory and manufacturing activities for these drugs either themselves or through third-party providers. As such, Ionis incurred all of the expenses associated with these activities and reported them in its consolidated financial statements. Ionis formed Akcea as a wholly owned subsidiary to complete development of and commercialize Ionis' drugs to treat lipid disorders. We began business operations in January 2015.

We exclusively licensed our pipeline of four novel drugs from Ionis effective in January 2015. Prior to then, Ionis had been advancing these drugs in development and incurring the expenses for those activities. Under our license agreement with Ionis, Ionis continued and is continuing to conduct development, regulatory and manufacturing activities for our drugs and charge us for this work. In this way, we benefit from Ionis' more than 25 years of experience developing and manufacturing antisense drugs. As we build our development, regulatory and manufacturing capabilities and capacity, we expect to assume increasing responsibility for these functions and Ionis' responsibilities will decrease. We expect that our collaborative approach will allow us to build these capabilities and capacity while still working closely with Ionis to help ensure a smooth transition as our drugs advance. Moreover, because Ionis is currently conducting the majority of the development activities for our drugs, we are focused on building the commercial organization and conducting the pre-commercialization activities necessary to support the launch of volanesorsen, if approved, for marketing.

We pay Ionis for the research and development expenses it incurs on our behalf, which include both external and internal expenses in accordance with our license agreement with Ionis. External research and development expenses include costs for contract research organizations, or CROs, costs to conduct nonclinical and clinical studies on our drugs, costs to acquire and evaluate clinical study data such as investigator grants, patient screening fees and laboratory work, and fees paid to consultants. Internal development expenses include costs for the work that Ionis' development employees perform for us. Ionis charges us a full-time equivalent rate that covers personnel-related expenses, including salaries and benefits, plus an allocation of facility-related expenses, including rent, utilities, insurance and property taxes, for those research and development employees who work either directly or indirectly on the development of our drugs. In accordance with the license agreement, we pay Ionis for external research and development expenses and internal research and development expenses. We also pay Ionis for the active pharmaceutical ingredient, or API, and drug product we use in our nonclinical and clinical studies for all of our drugs. Ionis manufactures the API for us and charges us a price per gram consistent with the price Ionis charges its pharmaceutical partners, which includes the cost for direct materials, direct labor and overhead required to manufacture the API. If we need the API filled in vials or pre-filled syringes for our clinical studies, Ionis will contract with a third party to perform this work and Ionis will charge us for the resulting cost.

Under the services agreement, Ionis also provides us certain services, including, without limitation, general and administrative support services and development support services. We pay Ionis for our share of the internal and external expenses for each of these functions based on our relative use of each function, plus an allocation of facility-related expenses. As our business grows and we assume increasing responsibility from Ionis, we will assume direct responsibility for procuring and financing the services we currently receive from Ionis and Ionis' responsibility to provide us with these services will decrease.

We do not pay a mark-up or profit on the external or internal expenses Ionis bills to us or on the cost of the drugs Ionis manufactures for us. Moreover, Ionis only charges us for the portion of its resources that we use. For example, we do not have to pay for a full time person if we only need the person's skills for 50% of the time. In this way, we can increase our headcount as our requirements grow and as we assume increasing responsibility for our drugs from Ionis, rather than building capabilities and capacity in advance of full utilization. We believe that our expenses reasonably reflect the expenses we would have incurred if we had the capabilities and capacity in place to perform this work ourselves. Further, we do not believe that our expenses will increase significantly as we assume development, regulatory, manufacturing and administrative responsibilities from Ionis because we will only assume these functions when we believe we can do so in a cost-efficient manner. See note 5, *Development, Commercialization and License Agreement and Services Agreement with Ionis*, to our condensed consolidated financial statements for more information on our agreements with Ionis.

In addition, Ionis has helped fund our operations through a line of credit agreement for up to $150.0 million that we entered into in January 2017. As of June 30, 2017, we had borrowed an aggregate of $106.0 million pursuant to the line of credit, which together with accrued interest automatically converted upon closing of our IPO into an aggregate of 13,438,339 shares of our common stock. Following the closing of our IPO, we no longer have access to the line of credit with Ionis.

Key Achievements

- We submitted a marketing authorization application, or MAA, to the European Medicines Agency, or EMA, for the approval of volanesorsen for the treatment of patients with FCS.
- We raised over $190 million in our IPO, including the underwriters' full exercise of their overallotment option, Novartis' $50 million strategic investment and $25 million strategic investment from Ionis, who discovered and is co-developing the drugs in our pipeline. Our IPO generated over $180 million in net proceeds.
- We established a strategic collaboration with Novartis, a leader in cardiovascular medicines, worth up to more than $1.6 billion plus royalties for the development and commercialization of AKCEA-APO(a)-L$_{Rx}$ and AKCEA-APOCIII-L$_{Rx}$ for large populations of patients who have high cardiovascular risk due to inadequately treated lipid disorders.
- We successfully completed the Phase 3 program of volanesorsen for the treatment of FCS.
- We expanded our independent board of directors with the appointments of Elaine Hochberg, Sandford Smith, Edward Fitzgerald and Christopher Gabrieli, as chairman of our board.
- We initiated a Phase 2b dose-ranging study with AKCEA-APO(a)-L$_{Rx}$ in patients with elevated Lp(a) and established cardiovascular disease to support the design of the Phase 3 cardiovascular outcome study.
- We published key preclinical findings with angiopoietin-like 3 (ANGPTL3)-targeting drugs and Phase 1/2 clinical study results with AKCEA-ANGPTL3-L$_{Rx}$ in the *New England Journal of Medicine.*
- We published results from the IN-FOCUS (Investigation of Findings and Observations Captured in Burden of Illness Survey in FCS Patients) survey, the largest survey in patients with FCS, demonstrating the considerable daily and life-long burden of disease for these patients.

Critical Accounting Policies

We prepare our condensed consolidated financial statements in conformity with accounting principles generally accepted in the United States. As such, we make certain estimates, judgments and assumptions that we believe are reasonable, based upon the information available to us. These judgments involve making estimates about the effect of matters that are inherently uncertain and may significantly impact our quarterly or annual results of operations and financial condition. Each quarter, our senior management reviews the development, selection and disclosure of such estimates with our audit committee of our board of directors. In the following paragraphs, we describe the specific risks associated with these critical accounting policies and we caution that future events rarely develop exactly as one may expect, and that best estimates may require adjustment.

The significant accounting policies, which we believe are the most critical to aid in fully understanding and evaluating our reported financial results, require the following:

- Assessing the propriety of revenue recognition and associated deferred revenue;
- Determining the proper valuation of investments in marketable securities;
- Determining the stock-based compensation expense and valuation assumptions;
- Determining the fair value of our common stock; and
- Determining the appropriate cost estimates for unbilled preclinical and clinical development activities.

These critical accounting policies and estimates are included in the financial statements and accompanying notes thereto for the fiscal year ended December 31, 2016 and the related Management's Discussion and Analysis of Financial Condition and Results of Operations, which are contained in our final prospectus dated July 13, 2017, filed with the SEC on July 14, 2017 pursuant to Rule 424(b)(4) under the Securities Act in connection with our IPO. There have been no material changes to these critical accounting policies and estimates.

Results of Operations

Revenue

During the three and six months ended June 30, 2017, we recognized $14.1 million and $23.7 million, respectively, in research and development revenue from our collaboration with Novartis, which we initiated in January 2017.

Operating Expenses

Operating expenses were $25.4 million and $94.9 million for the three and six months ended June 30, 2017 and increased compared to $13.7 million and $29.7 million for the same periods in 2016. Our operating expenses increased primarily due to sublicensing expenses paid to Ionis related to our collaboration with Novartis of which $33.4 million was non-cash, and development activities including the initiation of a Phase 2b dose-ranging study of AKCEA-APO(a)-L_{Rx}. As this year progresses, we expect our general and administrative expenses to increase as we continue to prepare to launch volanesorsen.

In order to analyze and compare our results of operations to other similar companies, we believe it is important to exclude non-cash compensation expense related to equity awards from our operating expenses. We believe non-cash compensation expense is not indicative of our operating results or cash flows from our operations. Further, we internally evaluate the performance of our operations excluding it.

Research and Development Expenses

The following table sets forth our research and development expenses for the periods presented (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	2016	2017	2016
External volanesorsen expenses	$ 6,401	$ 4,823	$ 12,004	$ 10,160
Other external research and development project expenses	5,394	1,912	10,304	4,543
Sublicensing expenses	—	—	48,394	—
Research and development personnel and overhead expenses	4,773	2,898	9,060	5,884
Total research and development expenses, excluding non-cash stock-based compensation expense	16,568	9,633	79,762	20,587
Non-cash stock-based compensation expense	1,919	1,311	3,520	2,147
Total research and development expenses	$ 18,487	$ 10,944	$ 83,282	$ 22,734

Research and development expenses were $16.6 million and $79.8 million for the three and six months ended June 30, 2017, respectively, and increased compared to $9.6 million and $20.6 million for the same periods in 2016. The increase in expenses was primarily due to sublicensing expenses incurred in the first quarter of 2017, the majority of which were non-cash, related to our collaboration with Novartis, and the progression of our other drugs in development, including AKCEA-APO(a)-L_{Rx}, AKCEA-APOCIII-L_{Rx} and AKCEA-ANGPTL3-L_{Rx} during the first half of 2017. All amounts exclude non-cash compensation expense related to equity awards.

General and Administrative Expenses

The following table sets forth our general and administrative expenses for the periods presented (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	2016	2017	2016
General and administrative support expenses	$ 2,308	$ 1,415	$ 3,884	$ 2,620
Pre-commercialization expenses for volanesorsen	2,584	680	4,104	1,373
Total general and administrative expenses, excluding non-cash stock-based compensation expense	4,892	2,095	7,988	3,993
Non-cash stock-based compensation expense	2,023	667	3,602	3,021
Total general and administrative expenses	$ 6,915	$ 2,762	$ 11,590	$ 7,014

General and administrative expenses were $4.9 million and $8.0 million for the three and six months ended June 30, 2017, respectively, and increased compared to $2.1 million and $4.0 million for the same periods in 2016. Our general and administrative expenses increased primarily because we were continuing to build the commercial organization and advance pre-commercialization activities necessary to launch volanesorsen, if approved for marketing. All amounts exclude non-cash compensation expense related to equity awards.

Liquidity and Capital Resources

At June 30, 2017, we had cash, cash equivalents and short-term investments of $118.7 million and stockholders' deficit of $83.0 million.

We have funded our operating activities through a $100.0 million cash contribution that we received from Ionis in 2015, $75.0 million from initiating our collaboration with Novartis that we received in the first quarter of 2017 and $106.0 million in drawdowns under our line of credit with Ionis that we received in the first and second quarters of 2017. Our borrowings under our line of credit agreement with Ionis converted into shares of our common stock at the IPO price in connection with the closing of our IPO in July 2017. We no longer have access to the line of credit. We received $182.4 million in net proceeds from the IPO and the Novartis concurrent private placement in July 2017, including $25.0 million from Ionis' participation in our IPO.

At June 30, 2017, we had working capital of $53.6 million, compared to working capital of $(19.3) million at December 31, 2016. Working capital increased in 2017 primarily due to the increase in our cash and short-term investments and a decrease in our payable to Ionis under our development, commercialization and license agreement and services agreement. As of June 30, 2017, our outstanding payable to Ionis was $11.2 million. In January 2017, we initiated a strategic collaboration with Novartis and we received $75.0 million in an upfront option payment, of which we retained $60.0 million and paid Ionis $15.0 million as a sublicense fee under our license agreement with Ionis, in May 2017. During the first half of 2017, we recognized $23.7 million in research and development revenue from our collaboration with Novartis.

We do not currently have any approved drugs and, therefore, we do not expect to generate significant revenue from drug sales unless and until we or our partners obtain regulatory approval for and commercialize volanesorsen or one of our other drugs in development. We anticipate that we will continue to incur losses for the foreseeable future, and we expect the losses to increase as we continue to develop, seek regulatory approval for, and begin to commercialize our drugs. We are subject to all of the risks incident in developing and commercializing new drugs, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business.

Future Funding Requirements

We will need to raise additional funding in the future to continue developing the drugs in our pipeline and to commercialize any approved drug, including volanesorsen. We believe that the net proceeds from our IPO and the concurrent private placement, together with our existing cash, cash equivalents and short-term investments, will be sufficient to fund our operations for at least the next 12 months. Until such time, if ever, as we can generate substantial product revenue, we may finance our cash needs through additional financing in the future through the issuance of our common stock, through other equity or debt financings or through collaborations or partnerships with other companies. In any event, we may not generate significant revenue from product sales prior to the use of the net proceeds from our IPO and the concurrent private placement. We do not have any committed external source of funds and we no longer have access to our line of credit. Additional capital may not be available on reasonable terms, if at all. To the extent that we raise additional capital through the sale of stock or convertible debt securities, the ownership interest of our stockholders 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 increased fixed payment obligations and covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, declaring dividends, selling or licensing intellectual property rights and other operating restrictions that could adversely affect our ability to conduct our business. If we raise additional funds through collaborations or licensing arrangements with third parties, we may have to relinquish valuable rights to our drugs or grant licenses on terms that may not be favorable to us. If we cannot raise additional funds through stock offerings or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and commercialize our drugs even if we would otherwise prefer to develop and commercialize the drugs ourselves.

Our forecast of the period of time through which our financial resources will be adequate to support our operations involves risks and uncertainties, and actual results could vary as a result of a number of factors. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. The amount and timing of future funding requirements, both near- and long-term, will depend on many factors, including, but not limited to:

- the design, initiation, progress, size, timing, costs and results of our clinical and nonclinical studies;
- the outcome, timing and cost of regulatory approvals by the FDA and comparable foreign regulatory authorities, including the potential for the FDA or comparable foreign regulatory authorities to require that we perform more studies than, or evaluate clinical endpoints other than, those that we currently expect;
- the number and characteristics of drugs that we may pursue;
- our need to expand our development activities, including our need and ability to hire additional employees;
- the effect of competing technological and market developments;
- the cost of establishing sales, marketing, manufacturing and distribution capabilities for our drugs;
- our strategic collaborators' success in developing and commercializing our drugs;
- our need to add infrastructure, implement internal systems and hire additional employees to operate as a public company; and
- the revenue, if any, generated from commercial sales of our drugs for which we receive marketing authorization, which may be affected by market conditions, including obtaining coverage and adequate reimbursement of our drugs from third-party payors, including government programs and managed care organizations, and competition within the therapeutic class to which our drugs are assigned.

If we cannot expand our operations or otherwise capitalize on our business opportunities because we lack sufficient capital, our business, financial condition and results of operations could be materially adversely affected.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of June 30, 2017, which consist of our operating lease for our office facility. The table provides a breakdown of when our office facility lease obligations become due (in thousands):

Contractual obligations	Total	Less than 1 year	1 - 2 years	3 - 5 years
Office facility operating lease payments	$ 1,147	$ 655	$ 283	$ 209

We have not included potential milestone payments, sublicense fees and royalties that we may be required to pay Ionis for the license of intellectual property. We have not included these potential obligations in the table above because they are contingent upon the occurrence of future events, and we do not know the timing and likelihood of such potential obligations with certainty.

The table above does not include certain general and administrative and development support services for which we will pay Ionis under our services agreement or obligations under agreements that we can cancel without a significant penalty.

We describe our agreements with Ionis in more detail in note 5, *Development, Commercialization and License Agreement and Services Agreement with Ionis*, to our condensed consolidated financial statements.

In addition to contractual obligations, we had outstanding purchase orders as of June 30, 2017 and December 31, 2016 for the purchase of services and materials as part of our normal course of business.

Off-balance Sheet Arrangements

We did not have any off-balance sheet arrangements during the period presented, as defined in the rules and regulations of the SEC.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below, together with all of the other information in this prospectus, including our consolidated financial statements and related notes, before deciding whether to purchase shares of our common stock. If any of the following risks are realized, our business, operating results and prospects could be materially and adversely affected. In that event, the price of our common stock could decline, and you could lose part or all of your investment. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also adversely affect our business. We have marked with an asterisk those risk factors that reflect substantive changes from the risk factors included in our financial statements and accompanying notes thereto for the fiscal year ended December 31, 2016, which are contained in our final prospectus dated July 13, 2017, filed with the SEC on July 14, 2017 pursuant to Rule 424(b) under the Securities Act, in connection with our IPO.

Risks Related to Our Financial Condition and Need for Additional Capital

We have a limited operating history and may never become profitable.

Ionis Pharmaceuticals, Inc., or Ionis, incorporated us as a Delaware corporation in December 2014, and we have operated as a subsidiary of Ionis since that time. As such, we have limited experience as a company, and no experience operating independently from Ionis, and have not yet demonstrated that we can successfully overcome many of the risks and uncertainties frequently encountered in new and rapidly evolving fields, particularly the biotechnology and pharmaceutical fields.

As a company, we have never obtained regulatory approval for, or commercialized, any product. Our ability to generate substantial revenue and achieve profitability depends on our ability, alone or with strategic partners, to successfully develop our drugs, and obtain the regulatory approvals necessary to commercialize our drugs, including volanesorsen, AKCEA-APO(a)-L_{Rx} and our other drugs in development. We do not anticipate generating revenue from product sales for at least the next few years, if ever. Even if we achieve profitability in the future, we may not sustain profitability in subsequent periods. Our ability to generate revenue from product sales depends heavily on our and our current and future strategic partners' success in:

- completing clinical development of volanesorsen for one or more indications and nonclinical and clinical development of AKCEA-APO(a)-L_{Rx}, AKCEA-ANGPTL3-L_{Rx} and AKCEA-APOCIII-L_{Rx};
- seeking and obtaining regulatory and marketing authorization for our drugs, including volanesorsen, AKCEA-APO(a)-L_{Rx} and our other drugs in development;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide the amount and quality of products and services we need to continue to develop and, if approved, commercialize volanesorsen, AKCEA-APO(a)-L_{Rx} and our other drugs in development;
- launching and commercializing volanesorsen and AKCEA-ANGPTL3-L_{Rx} by establishing a sales, marketing and distribution infrastructure;
- launching and co-commercializing AKCEA-APO(a)-L_{Rx} and AKCEA-APOCIII-L_{Rx} through our collaboration with Novartis Pharma AG, or Novartis, under terms that we plan to negotiate with Novartis in the future;
- educating physicians about our target patient populations, including patients with familial chylomicronemia syndrome, or FCS, and patients with familial partial lipodystrophy, or FPL;
- obtaining market acceptance of volanesorsen, AKCEA-APO(a)-L_{Rx} and our other drugs in development as viable treatment options;
- obtaining and maintaining adequate coverage and reimbursement from third-party payors for volanesorsen, AKCEA-APO(a)-L_{Rx} and our other drugs in development;
- addressing any competing technological and market developments;
- implementing additional internal systems and infrastructure, as needed, to ultimately operate without reliance on Ionis;
- negotiating favorable terms in any partnership, licensing or other arrangements into which we may enter;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, product trademarks and know-how;
- developing and commercializing volanesorsen, AKCEA-APO(a)-L_{Rx} and our other drugs in development without infringing others' intellectual property rights; and
- attracting, hiring and retaining qualified personnel.

We may not successfully develop any products, generate product revenue or achieve profitability. If we cannot achieve or maintain profitability, it would depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. If the market price of our common stock declined, you could lose all or part of your investment.

We have incurred losses since our inception.*

Because drug discovery and development require substantial lead-time and funding prior to commercialization, we have incurred expenses while generating limited revenue from our operating activities since our formation. Our net losses were $83.2 million, $61.4 million and $30.0 million for the years ended December 31, 2016, December 31, 2015 and December 31, 2014, respectively. Our net losses were $72.3 million and $29.6 million for the six months ended June 30, 2017 and 2016, respectively. As of June 30, 2017, we had an accumulated deficit of approximately $83.0 million. Most of the losses resulted from costs incurred in connection with our development programs and from general and administrative costs associated with our operations. We expect to incur additional operating losses for the foreseeable future, and these losses may increase if we cannot generate substantial revenue.

We will require substantial additional funding to achieve our goals. If we fail to obtain timely funding, we may need to curtail or abandon some of our programs.*

All of our drugs are undergoing clinical studies. All of our drug programs will require additional nonclinical and/or clinical testing and/or marketing authorization prior to commercialization. We will need to spend significant additional resources to conduct these activities. Our expenses could increase beyond expectations if the U.S. Food and Drug Administration, or FDA, the European Medicines Agency, or EMA, or other regulatory authorities require us to perform clinical studies and other studies in addition to those that we currently anticipate. As of June 30, 2017, we had cash, cash equivalents and short-term investments equal to $118.7 million. Our research and development expenses were $68.5 million, $50.9 million and $29.0 million for the years ended December 31, 2016, December 31, 2015 and December 31, 2014, respectively. Our research and development expenses were $83.3 million and $22.7 million for the six months ended June 30, 2017 and 2016, respectively.

We have funded our operating activities through a $100.0 million cash contribution we received from Ionis in 2015, $75.0 million we received from initiating our collaboration with Novartis and $106.0 million in drawdowns under our line of credit with Ionis. The line of credit converted to our common stock when we closed our IPO. We no longer have access to the line of credit following the closing of our IPO and we do not have any firm commitment from Ionis to fund our cash flow deficits or provide other direct or indirect financial assistance to us. Based on our existing cash, cash equivalents and short-term investments and the proceeds from our IPO and the concurrent private placement with Novartis, we will need to raise additional funding to continue developing the drugs in our pipeline and to seek regulatory approval for and to commercialize volanesorsen and other drugs in our pipeline.

Even if we obtain marketing authorizations to sell volanesorsen or AKCEA-ANGPTL3-L_{Rx}, we will incur significant costs to commercialize the approved product. Even if we generate revenue from the sale of any approved products, we may not become profitable and would need to obtain additional funding to continue operations.

Risks Related to Clinical Development, Regulatory Review and Approval of Our Drugs

If the results of clinical testing indicate that any of our drugs are not suitable for commercial use we may need to abandon one or more of our drug development programs.

Drug discovery and development has inherent risks and the historical failure rate for drugs is high. Antisense drugs are a relatively new approach to therapeutics. If we cannot demonstrate that our drugs are safe and effective for human use in the intended indication, we may need to abandon one or more of our drug development programs.

If any of our drugs in clinical studies, including volanesorsen, AKCEA-APO(a)-L_{Rx} and our other drugs in development, do not show sufficient safety and efficacy in patients with the targeted indication, it would negatively affect our development and commercialization goals for the drug and we would have expended significant resources with little or no benefit to us.

Even if our drugs are successful in preclinical and earlier-stage clinical studies, the drugs may not be successful in later-stage clinical studies.

Successful results in preclinical or initial clinical studies, including the results of earlier studies for our drugs in development, may not predict the results of subsequent clinical studies, including the Phase 3 study of volanesorsen for the treatment of FPL. There are a number of factors that could cause a clinical study to fail or be delayed, including:

- the clinical study may produce negative or inconclusive results;
- regulators may require that we hold, suspend or terminate clinical research for noncompliance with regulatory requirements;
- we, our partners, the FDA or foreign regulatory authorities could suspend or terminate a clinical study due to adverse side effects of a drug on people in the study;
- we or our partners may decide, or regulators may require us, to conduct additional preclinical testing or clinical studies;
- we or our partners may not identify, recruit and train suitable clinical investigators at a sufficient number of study sites;
- the institutional review board for a prospective site might withhold or delay its approval for the study;
- enrollment in our clinical studies may be slower than we anticipate;
- patients who enroll in the clinical study may later drop out due to adverse events, a perception they are not benefiting from participating in the study, fatigue with the clinical study process or personal issues;
- a clinical study site may deviate from the protocol for the study;
- the cost of our clinical studies may be greater than we anticipate;
- we or our partners may require additional capital to fund the clinical study; and
- the supply or quality of our drugs or other materials necessary to conduct the clinical studies may be insufficient, inadequate or delayed.

In addition, volanesorsen and AKCEA-APOCIII-L_{Rx} have the same mechanism of action, and all of our current drugs, including volanesorsen, AKCEA-APO(a)-L_{Rx}, AKCEA-ANGPTL3-L_{Rx} and AKCEA-APOCIII-L_{Rx}, are chemically similar to each other and the drugs Ionis and other companies are developing separately. As a result, a safety observation we, Ionis or other companies encounter with one of our or their drugs could have or be perceived by a regulatory authority to have an impact on a different drug we are developing. This could cause the FDA and other regulators to ask questions or take actions that could harm or delay our ability to develop and commercialize our drugs or increase our costs. For example, the FDA or other regulatory agencies could request, among other things, any of the following regarding one of our drugs: additional information or commitments before we can start or continue a clinical study, protocol amendments, increased safety monitoring, additional product labeling information, and post-approval commitments. Similarly, we have an ongoing Phase 3 study of volanesorsen in patients with FPL and an ongoing open label extension study of volanesorsen in patients with FCS. Adverse events or results from these studies could negatively impact our planned marketing approval applications for volanesorsen in patients with FCS or the commercial opportunity for volanesorsen.

Any failure or delay in the clinical studies for any of our drugs in development could reduce the commercial potential or viability of our drugs.

We may not have appropriately designed the planned and ongoing clinical studies for volanesorsen, AKCEA-APO(a)-L_{Rx} and our other drugs in development to support submission of a marketing application to the FDA and foreign regulatory authorities or demonstrate safety or efficacy at the level required by the FDA and foreign regulatory authorities for product approval.

We recently completed a Phase 3 clinical program for volanesorsen for the treatment of FCS and have an ongoing Phase 3 study of volanesorsen in patients with FPL. We are also conducting or plan to conduct clinical studies for AKCEA-APO(a)-L_{Rx}, AKCEA-ANGPTL3-L_{Rx} and AKCEA-APOCIII-L_{Rx}.

Even if we achieve positive results on the endpoints for these clinical studies or any future clinical studies, the FDA or foreign regulatory authorities may believe the clinical studies do not show the appropriate balance of safety and efficacy in the indication being sought or may interpret the data differently than we do, and deem the results insufficient to demonstrate the appropriate balance of safety and efficacy at the level required for product approval. For example, the FDA or foreign regulatory authorities could claim that we have not tested volanesorsen in a sufficient number of patients to demonstrate volanesorsen is safe and effective in patients with FCS or FPL to support an application for marketing authorization. In such a case, we may need to conduct additional clinical studies before obtaining marketing authorization, which would be expensive and delay these development programs. These risks are more likely to occur since we are developing our drugs against therapeutic targets or to treat diseases in which there is little or no clinical experience. In addition, these risks may be more likely to occur for volanesorsen since three of the patients in the Phase 3 program experienced serious platelet events (grade 4 thrombocytopenia), a condition in which the patient has very low platelet levels, and additional patients experienced other adverse events in the program, including five patients who discontinued participation in the APPROACH study due to platelet count declines.

We may make modifications to the clinical study protocols or designs of our ongoing clinical studies that delay enrollment or completion of such clinical studies and could delay regulatory approval of volanesorsen and our other drugs in development. Any failure to obtain approval for volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development on the timeline that we currently anticipate, or at all, would have a material and adverse impact on our business, prospects, financial condition and results of operations and could cause our stock price to decline.

If we or our partners fail to obtain regulatory approval for our drugs, including volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development, we or our partners cannot sell them in the applicable markets.

We cannot guarantee that any of our drugs, including volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development, will be safe and effective, or will be approved for commercialization. We and our partners must conduct time-consuming, extensive and costly clinical studies to demonstrate the safety and efficacy of each of our drugs, including volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development, before they can be approved for sale. We and our partners must conduct these studies in compliance with FDA regulations and with comparable regulations in other countries.

We or our partners may not obtain necessary regulatory approvals on a timely basis, if at all, for any of our drugs. It is possible that regulatory authorities will not approve any of our drugs, including volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development, for marketing. If the FDA or another regulatory authority believes that we or our partners have not sufficiently demonstrated the safety or efficacy of any of our drugs, including volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development, the authority will not approve the specific drug or will require additional studies, which can be time consuming and expensive and which will delay or harm our ability to successfully commercialize the drug. For example, since three of the patients in the Phase 3 program for volanesorsen experienced serious platelet events (grade 4 thrombocytopenia), a condition in which the patient has very low platelet levels, and additional patients experienced other adverse events in the program, some of whom discontinued participation in the studies, including five patients who discontinued participation in the APPROACH study due to platelet count declines, the FDA or another regulatory authority may require us to conduct additional studies of volanesorsen before considering an application for marketing approval.

The FDA or other comparable foreign regulatory authorities can delay, limit or deny approval of a drug for many reasons, including:

- such authorities may disagree with the design or implementation of our clinical studies;
- we or our partners may be unable to demonstrate to the satisfaction of the FDA or other regulatory authorities that a drug is safe and effective for any indication;
- such authorities may not accept clinical data from studies conducted at clinical facilities that have deficient clinical practices or that are in countries where the standard of care is potentially different from the United States;
- we or our partners may be unable to demonstrate that our drug's clinical and other benefits outweigh its safety risks to support approval;
- such authorities may disagree with the interpretation of data from preclinical or clinical studies;
- such authorities may find deficiencies in the manufacturing processes or facilities of third-party manufacturers who manufacture clinical and commercial supplies for our drugs; and
- the approval policies or regulations of such authorities or their prior guidance to us or our partners during clinical development may significantly change in a manner rendering our clinical data insufficient for approval.

Failure to successfully develop volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development, or to receive marketing authorization for these drugs or delays in these authorizations would prevent or delay the commercial launch of the drug, and, as a result, would negatively affect our ability to generate revenue.

We may not be able to benefit from orphan drug designation for volanesorsen, or any of our other drugs.

The FDA and EMA have granted orphan drug designation to volanesorsen for the treatment of patients with FCS. The EMA has granted orphan drug designation to volanesorsen for the treatment of patients with FPL and we are in the process of applying for orphan drug status for FPL in the United States. In the United States, under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process, but it can provide financial incentives, such as tax advantages and user-fee waivers, as well as longer regulatory exclusivity periods.

We may lose orphan drug exclusivity if the FDA determines that the request for designation was materially defective or if we cannot assure sufficient quantity of the applicable drug to meet the needs of patients with the rare disease or condition.

Even if we maintain orphan drug exclusivity for volanesorsen or obtain orphan drug exclusivity for our other drugs, the exclusivity may not effectively protect the drug from competition because regulatory authorities still may authorize different drugs for the same condition.

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

We are dedicating a substantial amount of our resources to develop and seek regulatory approval for volanesorsen to treat patients with FCS and FPL. As a result, we may forego or delay pursuit of opportunities with our other drugs or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future research and development programs and drugs for specific indications may not yield any commercially viable drugs.

Our drugs, including volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development, could be subject to regulatory limitations following approval.

Following approval of a drug, we and our partners must comply with comprehensive government regulations regarding the manufacture, marketing and distribution of drug products. Promotional communications regarding prescription drugs must be consistent with the information in the product's approved labeling. We and our partners may not obtain the labeling claims necessary or desirable to successfully commercialize our drug products, including volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development.

The FDA and foreign regulatory authorities can impose significant restrictions on an approved drug product through the product label and on advertising, promotional and distribution activities.

In addition, when approved, the FDA or a foreign regulatory authority may condition approval on the performance of post-approval clinical studies or patient monitoring, which could be time consuming and expensive. If the results of such post-marketing studies are not satisfactory, the FDA or a foreign regulatory authority may withdraw marketing authorization or may condition continued marketing on commitments from us or our partners that may be expensive and/or time consuming to fulfill.

In addition, if we or others identify side effects after any of our drug products are on the market, if manufacturing problems occur subsequent to regulatory approval, or if we, our manufacturers or our partners fail to comply with regulatory requirements, we or our partners could be subject to:

- restrictions on our ability to conduct clinical studies, including full or partial clinical holds on ongoing or planned clinical studies;
- restrictions on such products' manufacturing processes;
- changes to the product label;
- restrictions on the marketing of a product;
- restrictions on product distribution;
- requirements to conduct post-marketing clinical studies;
- Untitled or Warning Letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenue;
- suspension or withdrawal of regulatory approvals;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions; or
- imposition of civil or criminal penalties.

Any one or a combination of these events could prevent us from achieving or maintaining market acceptance of the affected drug product or could substantially increase the costs and expenses of commercializing such drug product, which in turn could delay or prevent us from generating any revenue or profit from the sale of the drug product.

Risks Related to Commercialization of Our Drugs

If we cannot establish effective marketing and sales capabilities or enter into agreements with third parties to market and sell our drug products, we may not generate product revenue.

We currently have a limited commercial infrastructure to market, sell or distribute our drugs. If approved, to commercialize our products, we must build our marketing, sales and distribution capabilities or make arrangements with third parties to perform these services. We may not be successful in doing so. To commercialize volanesorsen and AKCEA-ANGPTL3-L$_{Rx}$ in the initial indications we plan to pursue, we plan to build a specialty sales force in each global region we expect to market the applicable drug, supported by case managers, reimbursement specialists, partnerships with specialty pharmacies, injection training, routine platelet monitoring, dietary counseling and a medical affairs team. We may seek to further penetrate markets by expanding our sales force or through strategic partnerships with other pharmaceutical or biotechnology companies or third party sales organizations, such as our strategic collaboration with Novartis.

Even though certain members of our management team and other employees have significant experience commercializing drug products, as a company we have no prior experience marketing, selling or distributing drug products, and there are significant risks involved in building and managing a commercial infrastructure. It will be expensive and time consuming for us to build and establish our own sales force and related compliance protocols to market any drug products. We may never successfully develop this capability and any failure could delay or preclude a product launch. We and our partners, will have to compete with other companies to recruit, hire, train, manage and retain marketing and sales personnel.

We will incur expenses prior to product launch to develop a marketing and sales infrastructure. If regulatory requirements or other factors cause a delay in the commercial launch of volanesorsen, or our other drugs in development, we would incur additional expenses for having developed these capabilities earlier than required and prior to realizing any revenue from sales of volanesorsen and our other drugs in development. Even if we can effectively hire a sales force and develop a marketing and sales infrastructure, our sales force and marketing teams may not successfully commercialize volanesorsen or our other drugs in development.

If we cannot hire a sales force or collaborate with a third-party marketing and sales organization to globally commercialize any approved drug product, our ability to generate product revenue may be limited. To the extent we rely on third parties to commercialize any drug products, such as would be the case if Novartis exercises its option for AKCEA-APO(a)-L_{Rx} or AKCEA-APOCIII-L_{Rx}, we may receive less revenue than if we commercialized these drug products ourselves. In addition, we would have less control over the sales efforts of any other third parties involved in our commercialization efforts.

We plan to rely on third-party specialty channels to distribute volanesorsen, and our other drugs to patients. If we cannot effectively establish and manage this distribution process, it could harm or delay the commercial launch and sales of volanesorsen and our other drugs in development.

We and our strategic partners may contract with, and rely on, third-party specialty pharmacies to distribute volanesorsen, and our other drugs to patients. A specialty pharmacy is a pharmacy that specializes in dispensing medications for complex or chronic conditions, a process that requires a high level of patient education and ongoing management. Our management team will need to devote a significant amount of its attention to building and managing this distribution network. If we cannot effectively build and manage this distribution process, the commercial launch and sales of volanesorsen and AKCEA-ANGPTL3-L_{Rx} will be delayed or less successful, which would harm our results of operations.

In addition, the use of specialty pharmacies involves certain risks, including, but not limited to, risks that these organizations will:

- not provide us with accurate or timely information regarding their inventories, the number of patients who are using our drugs or complaints regarding our drugs;
- not effectively sell or support volanesorsen, AKCEA-ANGPTL3-L_{Rx} and our other drugs;
- reduce or discontinue their efforts to sell or support volanesorsen, AKCEA-ANGPTL3-L_{Rx} or our other drugs;
- not devote the resources necessary to sell volanesorsen, AKCEA-ANGPTL3-L_{Rx} or our other drugs in the volumes and within the time frames that we expect;
- not satisfy financial obligations to us or others; or
- cease operations.

Any such events may result in decreased sales and lower revenue, which could have a material adverse effect on our business, prospects, financial condition and results of operations.

If the market does not accept our drugs, including volanesorsen and our other drugs in development, we are not likely to generate substantial product revenue or become profitable.

Even if we or our strategic partners obtain a marketing authorization for volanesorsen and our other drugs in development, our success will depend upon the medical community, patients and third-party payors accepting our drugs as medically useful, cost-effective, safe and convenient. Even if the FDA or foreign regulatory authorities authorize our drugs for commercialization, doctors may not prescribe our drugs to treat patients. We and our partners may not successfully commercialize additional drugs.

Additionally, in many of the markets where we or our partners may sell our drugs in the future, if we cannot agree with the government or other third-party payors regarding the price we can charge for our drugs, then we may not be able to sell our drugs in that market. Similarly, cost control initiatives by governments or third-party payors could decrease the price received for our drugs or increase patient coinsurance to a level that makes commercializing volanesorsen, AKCEA-APO(a)-L_{RX} and our other drugs in development economically unviable.

The degree of market acceptance for volanesorsen, AKCEA-APO(a)-L_{Rx} and our other drugs in development depends upon a number of factors, including the:

- receipt and scope of marketing authorizations;
- establishment and demonstration in the medical and patient community of the efficacy and safety of our drugs and their potential advantages over competing products;
- cost and effectiveness of our drugs compared to other available therapies;
- patient convenience of the dosing regimen for our drugs; and
- reimbursement by government and third-party payors.

Based on the profile of our drugs, physicians, patients, patient advocates, payors or the medical community in general may not accept and/or use any drugs that we may develop. For example, we expect volanesorsen's product label will require periodic platelet monitoring, which could negatively affect our ability to attract and retain patients for volanesorsen. Additionally, in the clinical setting, some patients discontinued treatment with volanesorsen, including five patients who discontinued participation in the APPROACH study due to platelet count declines. While we believe we can better maintain patients on volanesorsen through our patient-centric commercial approach where we plan to have greater involvement with physicians and patients, if we cannot effectively maintain patients on volanesorsen, we may not be able to generate substantial revenue from volanesorsen sales.

The patient populations suffering from FCS and FPL are small and have not been established with precision. If the actual number of patients is smaller than we estimate, or if we cannot raise awareness of these diseases and diagnosis is not improved, our revenue and ability to achieve profitability may be adversely affected.

We estimate there are 3,000 to 5,000 FCS patients and an additional 3,000 to 5,000 FPL patients globally. Our estimates of the sizes of the patient populations are based on published studies as well as internal analyses. If the results of these studies or our analyses of them do not accurately reflect the number of patients with FCS and FPL, our assessment of the market potential for volanesorsen may be inaccurate, making it difficult or impossible for us to meet our revenue goals, or to obtain and maintain profitability. In addition, as is the case with most orphan diseases, if we cannot successfully raise awareness of these diseases and improve diagnosis, it will be more difficult or impossible to achieve profitability.

In addition, since the patient populations for FCS and FPL are small, the per-patient drug pricing must be high in order to recover our development and manufacturing costs, fund adequate patient support programs and achieve profitability. For these initial indications, we may not maintain or obtain sufficient sales volume at a price high enough to justify our product development efforts and our sales and marketing and manufacturing expenses.

If we or our partners fail to compete effectively, volanesorsen and our other drugs in development will not contribute significant revenue.

Our competitors engage in drug discovery throughout the world, are numerous and include, among others, major pharmaceutical companies and specialized biopharmaceutical firms. Our competitors may succeed in developing drugs that are:

- safer than our drugs;
- more effective than our drugs;
- priced lower than our drugs;
- reimbursed more favorably by government and other third-party payors than our drugs; or
- more convenient to use than our drugs.

These competitive developments could make our drugs, including volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development, obsolete or non-competitive. Further, all of our drugs are delivered by injection, which may render them less attractive to patients than non-injectable products offered by our current or future competitors.

Many of our competitors have substantially greater financial, technical and human resources than we do. In addition, many of these competitors have significantly greater experience than we do in conducting preclinical testing and human clinical studies, in obtaining FDA and other regulatory authorizations and in commercializing pharmaceutical products. Accordingly, our competitors may succeed in obtaining regulatory authorization for products earlier than we do. Marketing and sales capability is another factor relevant to the competitive position of our drugs, and many of our competitors will have greater marketing and sales capabilities than our capabilities.

There are several pharmaceutical and biotechnology companies engaged in the development or commercialization of products against targets that are also targets of drugs in our development pipeline. For example, if approved, volanesorsen could face competition from drugs like metreleptin. Metreleptin, produced by Novelion Therapeutics, Inc., is currently approved for use in generalized lipodystrophy patients. In September 2016, Arrowhead Pharmaceuticals, Inc. and Amgen Inc. announced a license and collaboration for development of Arrowhead's preclinical program which uses an RNAi conjugated with a GalNAc for the same target as AKCEA-APO(a)-L$_{Rx}$. AKCEA-APOCIII-L$_{Rx}$ may compete with gemcabene, an oral small molecule that reduces ApoC-III, that Gemphire Therapeutics, Inc. is developing to treat patients with triglycerides above 500 mg/dL. If volanesorsen or the other drugs in our pipeline cannot compete effectively with these and other products with common or similar indications to the drugs in our pipeline, we may not be able to generate substantial revenue from our product sales.

If government or other third-party payors fail to provide adequate coverage and payment rates for volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development, our revenue and prospects for profitability will be limited.

In both domestic and foreign markets, sales of our future products will depend in part upon the availability of coverage and reimbursement from third-party payors. The majority of patients in the United States who would fit within our target patient populations for our drugs have their healthcare supported by a combination of Medicare coverage, other government health programs such as Medicaid, managed care providers, private health insurers and other organizations. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. Assuming coverage is approved, the resulting reimbursement payment rates might not be enough to make our drugs affordable. Accordingly, volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development, if approved, will face competition from other therapies and drugs for limited financial resources. We may need to conduct post-marketing studies to demonstrate the cost-effectiveness of any future products to satisfy third-party payors. These studies might require us to commit a significant amount of management time and financial and other resources. Third-party payors may never consider our future products as cost-effective. Adequate third-party coverage and reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development.

Third-party payors, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In addition, in the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. Further, we believe that future coverage and reimbursement will likely be subject to increased restrictions both in the United States and in international markets. For example, in the United States, recent health reform measures have resulted in reductions in Medicare and other healthcare funding, and there have been several recent U.S. Congressional inquiries and proposed federal legislation designed to, among other things, reform government program reimbursement methodologies for drug products and bring more transparency to drug pricing. Third-party coverage and reimbursement for our products or drugs may not be available or adequate in either the United States or international markets, which would negatively affect the potential commercial success of our products, our revenue and our profits.

If we are found in violation of federal or state "fraud and abuse" laws or other healthcare laws and regulations, we may be required to pay a penalty and/or be suspended from participation in federal or state healthcare programs, which may adversely affect our business, financial condition and results of operation.

We may be subject to various federal and state laws pertaining to healthcare "fraud and abuse," including anti-kickback laws and false claims laws. Anti-kickback laws, among other things, make it illegal for a prescription drug manufacturer to pay, or offer to pay, a healthcare provider to refer, purchase or prescribe a particular drug. Due to the breadth of the statutory and regulatory provisions, it is possible that government authorities and others might challenge our practices under anti-kickback or other fraud and abuse laws. Moreover, recent healthcare reform legislation has strengthened these laws. In addition, false claims laws prohibit anyone from knowingly and willingly presenting, or causing to be presented for payment, to government third-party payors, including Medicare and Medicaid claims for reimbursed drugs that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. Our activities relating to the sale and marketing of our products may be subject to scrutiny under these laws. If we violated fraud and abuse laws, we could face a combination of:

- criminal and civil sanctions, including fines and civil monetary penalties;
- the possibility of exclusion from federal healthcare programs, including Medicare and Medicaid; and
- corporate integrity agreements, which could impose rigorous operational and monitoring requirements on us.

Given the significant penalties and fines that the government can impose on companies and individuals if convicted, allegations of violations often result in settlements even if the company or individual being investigated admits no wrongdoing. Settlements often include significant civil sanctions, including fines and civil monetary penalties, and corporate integrity agreements. If the government were to allege or convict us or our executive officers of violating these laws, our business could be harmed. In addition, private individuals may bring similar actions under the False Claims Act. Our activities could be subject to challenge for the reasons discussed above and due to the broad scope of these laws and the increasing focus on these laws by law enforcement authorities. To the extent we have access to protected health information we could be subject to federal and state health information privacy and security laws, including without limitation, the Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, which governs the conduct of certain electronic healthcare transactions and protects the security and privacy of protected health information. State health information privacy and security laws in certain circumstances are more stringent than HIPAA and many of the state laws differ from each other in significant ways and may not have the same effect, thus complicating compliance. Our failure to comply with applicable federal and state health information privacy and security laws could subject us to significant fines and multi-year corrective action plans. Once we have a commercialized drug, we will be required to report annually to Centers for Medicare and Medicaid Services certain information related to payments and other transfers of value we may provide to physicians and teaching hospitals. Further, an increasing number of state laws require manufacturers to make reports to states on pricing and marketing information. Many of these laws are unclear as to what is required to comply with the laws. Given the lack of clarity in laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent state authorities.

Similar rigid restrictions related to anti-kickbacks and promoting and marketing medicinal products apply in the European Union and other countries. Authorities in these countries strictly enforce these restrictions. Even in those countries where we will not be directly responsible for promoting and marketing our products, inappropriate activity by any of our international commercialization partners we may have could harm us.

Risks Related to Dependence on Third Parties

We plan to substantially depend on our collaboration with Novartis to develop and commercialize AKCEA-APO(a)-L$_{Rx}$ and AKCEA-APOCIII-L$_{Rx}$.

We have granted Novartis an exclusive option to exclusively license each of AKCEA-APO(a)-L$_{Rx}$ and AKCEA-APOCIII-L$_{Rx}$ pursuant to our strategic collaboration, option and license agreement with Novartis. We plan to substantially depend on Novartis to further develop and commercialize these drugs. We initiated this collaboration primarily to have Novartis:

- conduct the cardiovascular outcome studies that are likely to be required for approval of AKCEA-APO(a)-L$_{Rx}$ and AKCEA-APOCIII-L$_{Rx}$;
- seek and obtain regulatory approvals for AKCEA-APO(a)-L$_{Rx}$ and AKCEA-APOCIII-L$_{Rx}$; and
- globally commercialize AKCEA-APO(a)-L$_{Rx}$ and AKCEA-APOCIII-L$_{Rx}$.

If Novartis exercises its option to license one or both of these drugs, we would rely on Novartis to further develop, obtain regulatory approvals for, and commercialize the licensed drug. In general, we cannot control the amount and timing of resources that Novartis devotes to our strategic collaboration. If Novartis fails to use commercially reasonable effort to further develop, obtain regulatory approvals for, or commercialize these drugs, or if Novartis' efforts are not effective, our business may be negatively affected. Novartis could pursue other technologies or develop other drugs either on its own or in collaboration with others to treat the same diseases as we and Novartis plan to treat with AKCEA-APO(a)-L_{Rx} or AKCEA-APOCIII-L_{Rx}. Novartis could pursue these technologies and develop these other drugs at the same time as it is developing or commercializing AKCEA-APO(a)-L_{Rx} or AKCEA-APOCIII-L_{Rx}, and Novartis is not required to inform us of such activities.

Our strategic collaboration with Novartis may not continue for various reasons. Novartis can terminate our agreement at any time and is under no obligation to exercise the options we granted them. If Novartis does not exercise its option, or following option exercise stops developing or commercializing a drug, we will have to seek additional sources for funding and may have to delay or reduce our development and commercialization plans for AKCEA-APO(a)-L_{Rx} or AKCEA-APOCIII-L_{Rx}.

In addition, if Novartis exercises its option to license AKCEA-APO(a)-L_{Rx} or AKCEA-APOCIII-L_{Rx}, Novartis would be responsible for the long term supply of drug substance and finished drug product for the licensed drug.

Our strategic collaboration with Novartis may not result in the successful commercialization of AKCEA-APO(a)-L_{Rx} or AKCEA-APOCIII-L_{Rx}. If Novartis does not successfully develop, manufacture or commercialize AKCEA-APO(a)-L_{Rx} or AKCEA-APOCIII-L_{Rx}, we may receive limited or no revenues for these drugs.

AKCEA-APOCIII-L_{Rx} and AKCEA-ANGPTL3-L_{Rx} may compete with volanesorsen, which could reduce our expected revenues for volanesorsen.

Volanesorsen and AKCEA-APOCIII-L_{Rx} both inhibit the production of the same protein. We believe the enhancements we incorporated into AKCEA-APOCIII-L_{Rx} can provide greater patient convenience by allowing for significantly lower doses and less frequent administration compared to volanesorsen. As such, if Novartis exercises its option and successfully commercializes AKCEA-APOCIII-L_{Rx} while we are commercializing volanesorsen, to the extent physicians and patients elect to use AKCEA-APOCIII-L_{Rx} instead of volanesorsen, it will reduce the revenue we derive from volanesorsen. In addition, while AKCEA-ANGPTL3-L_{Rx} and volanesorsen use different mechanisms of action, if AKCEA-ANGPTL3-L_{Rx} can effectively lower triglyceride levels in FCS patients, it may likewise reduce the revenue we derive from volanesorsen.

If we cannot manufacture our drugs or contract with a third party to manufacture our drugs at costs that allow us to charge competitive prices to buyers, we will not be able to operate profitably.

To successfully commercialize volanesorsen, AKCEA-APO(a)-L_{Rx} and our other drugs in development, we will need to establish large-scale commercial manufacturing capabilities either on our own or through a third-party manufacturer. In addition, as our drug development pipeline matures, we will have a greater need for clinical study and commercial manufacturing capacity. We have no direct experience manufacturing pharmaceutical products of the chemical class represented by our drugs, called oligonucleotides, on a commercial scale for the systemic administration of a drug. We currently rely and expect to rely for the foreseeable future on Ionis' manufacturing capacity and efficiency to produce our oligonucleotide drugs, and our business could be negatively affected if Ionis ceased to provide us with this capability for any reason. In addition, there are a small number of suppliers for certain raw materials that we use to manufacture our drugs, and some of these suppliers will need to increase their scale of production to meet our projected needs for commercial manufacturing. Further, if we cannot continue to acquire raw materials from these suppliers on commercially reasonable terms or at all, we may be required to find alternative suppliers, which could be expensive and time consuming and negatively affect our ability to develop or commercialize our drugs in a timely manner or at all. We may not be able to manufacture our drugs at a cost or in quantities necessary to make commercially successful products.

We do not have long-term supply agreements for our drugs. We cannot guarantee that we will have a steady supply of drug to complete clinical studies, make registration batches for approval or satisfy market demand if commercialized at prices that are commercially acceptable. In addition, if we need to change manufacturers for any reason, we will need to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with verifying a new manufacturer could negatively affect our ability to develop drugs in a timely manner or within budget.

Also, manufacturers must adhere to the FDA's current Good Manufacturing Practices regulations and similar regulations in foreign countries, which the applicable regulatory authorities enforce through facilities inspection programs. Our contract manufacturers may not comply or maintain compliance with Good Manufacturing Practices, or similar foreign regulations. Non-compliance could significantly delay or prevent receipt of marketing authorization for our drugs, including authorizations for volanesorsen, AKCEA-APO(a)-L_{Rx} and our other drugs in development, or result in enforcement action after authorization that could limit the commercial success of our drugs, including volanesorsen, AKCEA-APO(a)-L_{Rx} and our other drugs in development.

We depend on third parties to conduct our clinical studies for our drugs and any failure of those parties to fulfill their obligations could adversely affect our development and commercialization plans.

We depend on independent clinical investigators, contract research organizations and other third-party service providers to conduct the clinical studies for our drugs and expect to continue to do so in the future. For example, we use clinical research organizations for the clinical studies for volanesorsen, AKCEA-APO(a)-L_{Rx} and our other drugs in development. We rely heavily on these parties for successful execution of our clinical studies, but do not control many aspects of their activities. For example, the investigators are not our employees. However, we are responsible for ensuring that these third parties conduct each of our clinical studies in accordance with the general investigational plan, approved protocols for the study and applicable regulations. Third parties may not complete activities on schedule or may not conduct our clinical studies in accordance with regulatory requirements or our stated protocols. The failure of these third parties to carry out their obligations or a termination of our relationship with these third parties could delay or prevent the development, marketing authorization and commercialization of our drugs, including authorizations for volanesorsen, AKCEA-APO(a)-L_{Rx} and our other drugs in development.

We may seek to form additional partnerships in the future with respect to volanesorsen, and our other drugs in development, and we may not realize the benefits of such partnerships.

Although we intend to develop and commercialize volanesorsen for patients with FCS and FPL ourselves, we may form partnerships, create joint ventures or collaborations or enter into licensing arrangements with third parties for the development and commercialization of our drugs in development. For example, we have granted Novartis an exclusive option to exclusively license AKCEA-APO(a)-L$_{Rx}$ and AKCEA-APOCIII-L$_{Rx}$. We face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Any delays in entering into new strategic partnership agreements related to our drugs could delay the development and commercialization of our drugs and reduce their competitiveness even if they reach the market. Moreover, we may not be successful in our efforts to establish a strategic partnership or other collaborative arrangement for any additional drugs because the potential partner may consider that our development pipeline is not advanced enough to justify a collaborative effort, or that volanesorsen and our other drugs in development do not have the requisite potential to demonstrate safety and efficacy in the target populations. In addition, we will need to mutually agree with Ionis on the terms of any sublicense to a third party for volanesorsen and our other drugs in development. If we cannot mutually agree on terms for a sublicense to a third party or if Ionis does not agree to a sublicense at all, it could delay our ability to develop and commercialize volanesorsen and our other drugs in development. Even if we are successful in establishing such a strategic partnership or collaboration, we cannot be certain that, following such a strategic transaction or collaboration, we will be able to progress the development and commercialization of the applicable drugs as envisioned, or that we will achieve the revenue that would justify such transaction. If we do not accurately evaluate the commercial potential or target market for a particular drug, we may relinquish valuable rights to that drug through future collaboration, licensing or other arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights.

Risks Related to Our Relationship with Ionis

Ionis controls the direction of our business, and the concentrated ownership of our common stock will prevent you and other stockholders from influencing significant decisions.

Ionis owns approximately 68% of the economic interest and voting power of our outstanding common stock. As long as Ionis beneficially controls a majority of the voting power of our outstanding common stock, it will generally be able to determine the outcome of all corporate actions requiring stockholder approval, including the election and removal of directors. Even if Ionis were to control less than a majority of the voting power of our outstanding common stock, it may influence the outcome of such corporate actions so long as it owns a significant portion of our common stock. If Ionis continues to hold its shares of our common stock, it could remain our controlling stockholder for an extended period of time or indefinitely.

Ionis' interests may not be the same as, or may conflict with, the interests of our other stockholders. You will not be able to affect the outcome of any stockholder vote while Ionis controls the majority of the voting power of our outstanding common stock. As a result, Ionis can control, directly or indirectly and subject to applicable law, all matters affecting us, including:

- any determination with respect to our business strategy and policies, including the appointment and removal of officers and directors;
- any determinations with respect to mergers, business combinations or disposition of assets;
- our financing and dividend policy;
- compensation and benefit programs and other human resources policy decisions;
- termination of, changes to or determinations under our development, commercialization and license agreement, which we refer to as the license agreement, and services agreement with Ionis;
- changes to any other agreements that may adversely affect us; and
- determinations with respect to our tax returns.

Because Ionis' interests may differ from ours or yours, actions that Ionis takes with respect to us, as our controlling stockholder, may not be favorable to us or you.

If Ionis sells a controlling interest in our company to a third party in a private transaction, you may not realize a change of control premium on shares of our common stock, and we may become subject to the control of a presently unknown third party.

Ionis owns a significant equity interest in our company. This means that Ionis could choose to sell some or all of its shares of our common stock in a privately negotiated transaction, which, if sufficient in size, could result in a change of control of our company.

Ionis' ability to privately sell its shares of our common stock, with no requirement for a concurrent offer to be made to acquire your shares of our common stock, could prevent you from realizing any change of control premium on your shares of our common stock that may otherwise accrue to Ionis on its private sale of our common stock. Additionally, if Ionis privately sells its significant equity interest in our company, we may become subject to the control of a presently unknown third party. Such third party may have conflicts of interest with those of other stockholders. In addition, if Ionis sells a controlling interest in our company to a third party, such a sale could negatively impact or accelerate any future indebtedness we may incur, and negatively impact any other commercial agreements and relationships, all of which may adversely affect our ability to run our business as described herein and may have a material adverse effect on our operating results and financial condition.

Certain of our directors and officers may have actual or potential conflicts of interest because of their positions with Ionis.

Stanley T. Crooke, Chairman of the Board and Chief Executive Officer for Ionis, and B. Lynne Parshall, Chief Operating Officer for Ionis, serve on our board of directors and retain their positions with Ionis. Similarly, Elizabeth L. Hougen, Chief Financial Officer for Ionis, serves as our Chief Financial Officer and retains her position with Ionis. In addition, these individuals own Ionis equity and Ionis equity awards. Ionis common stock, options to purchase Ionis common stock and other Ionis equity awards represent a significant portion of these individuals' net worth. Their position at Ionis and the ownership of any Ionis equity or equity awards creates, or may create the appearance of, conflicts of interest when we ask these individuals to make decisions that could have different implications for Ionis than the decisions have for us. In addition, our certificate of incorporation will provide for the allocation of certain corporate opportunities between us and Ionis. Under these provisions, neither Ionis or its other affiliates, nor any of their officers, directors, agents or stockholders, will have any obligation to present to us certain corporate opportunities. For example, a director of our company who also serves as a director, officer or employee of Ionis or any of its other affiliates may present to Ionis certain acquisitions, in-licenses, potential development programs or other opportunities that may be complementary to our business and, as a result, such opportunities may not be available to us. To the extent attractive corporate opportunities are allocated to Ionis or its other affiliates instead of to us, we may not be able to benefit from these opportunities.

The resources Ionis provides us under the license agreement and the services agreement may not be sufficient for us to operate as a standalone company, and we may experience difficulty in separating our resources from Ionis.

Because we have not operated separately from Ionis in the past, we may have difficulty doing so. We will need to acquire resources in addition to, and eventually in lieu of, those provided by Ionis to our company, and may also face difficulty in separating our resources from Ionis' resources and integrating newly acquired resources into our business. In addition, Ionis may prioritize its own research, development, manufacturing and other needs ahead of the services Ionis has agreed to provide us, or Ionis employees who conduct services for us may prioritize Ionis' interests over our interests. Our business, financial condition and results of operations could be harmed if we have difficulty operating as a standalone company, fail to acquire resources that prove to be important to our operations or incur unexpected costs in separating our resources from Ionis' resources or integrating newly acquired resources.

We will incur incremental costs as a standalone company.

Ionis currently performs or supports many important corporate functions for our company. Our consolidated financial statements reflect charges for these services on an allocation basis. Under our services agreement with Ionis we can use these Ionis services for a fixed term established on a service-by-service basis. However, we generally will have the right to terminate a service earlier if we give notice to Ionis. Partial reduction in the provision of any service requires Ionis' consent. In addition, either party will be able to terminate the agreement due to a material breach of the other party, upon prior written notice, subject to limited cure periods.

We will pay Ionis mutually agreed upon fees for these services, based on Ionis' costs of providing the services. Since we negotiated the services agreement in the context of a parent subsidiary relationship, the terms of the agreement, including the fees charged for the services, may be higher or lower than those that would be agreed to by parties bargaining at arm's length for similar services and may be higher or lower than the costs reflected in the allocations in our historical consolidated financial statements. Ionis will pass third party costs through to us at Ionis' cost. In addition, while Ionis provides us these services, our operational flexibility to modify or implement changes with respect to such services or the amounts we pay for them will be limited.

We may not be able to replace these services or enter into appropriate third-party agreements on terms and conditions, including cost, comparable to those that we will receive from Ionis under our services agreement. Additionally, after the agreement terminates, we may not sustain the services at the same levels or obtain the same benefits as when we were receiving such services and benefits from Ionis. When we begin to operate these functions separately, if we do not have our own adequate systems and business functions in place, or cannot obtain them from other providers, we may not operate our business effectively or at comparable costs, and our business may suffer. In addition, we have historically received informal support from Ionis, which may not be addressed in our services agreement. The level of this informal support will diminish and could end in the future.

We may not be able to fully realize the expected benefits of our license agreement with Ionis.

We have a development, commercialization and license agreement with Ionis. Pursuant to the license agreement, subject to certain restrictions, we and Ionis will share development responsibilities for volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development. We are paying for research and development costs and reimbursing Ionis for Ionis' employees supporting our development activities. Until we build or acquire our own capabilities to replace those Ionis is providing to us, particularly development, regulatory and manufacturing services, we will be heavily dependent on Ionis.

While we and Ionis intend the license agreement to bolster our capabilities, certain terms of the license agreement may limit our ability to achieve this expected benefit, including:

- a Joint Steering Committee, or JSC, comprising two senior members from our company and two senior members from Ionis, sets the development strategy for our drugs by mutual agreement. A Regulatory Sub-committee, established by the JSC and having equal membership from our company and Ionis, will set the regulatory strategy for each of our drugs by mutual agreement. If the JSC or the Regulatory Sub-committee cannot come to a mutual agreement, it could delay our ability to develop and commercialize volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development;

- we will need to mutually agree with Ionis on the terms of any additional sublicense to a third party for volanesorsen and our other drugs in development. If we cannot mutually agree on terms for a sublicense to a third party or if Ionis does not agree to a sublicense at all, it could delay or prevent our ability to develop and commercialize volanesorsen and our other drugs in development;
- we will need to obtain Ionis' approval to in-license a product, acquire a product or acquire another company, until the earlier of (i) 5 years following our IPO or (ii) when Ionis no longer is required to record its share of our profits and losses from an accounting perspective; and
- there is nothing in our agreements with Ionis to prevent Ionis from developing and commercializing drugs targeting RNAs that are not ApoC-III, Apo(a) or ANGPTL3 to pursue the same indications we are pursuing with our drugs.

Each of the foregoing terms and Ionis' other rights under the license agreement, could limit our ability to realize the expected benefits of the license agreement or otherwise limit our ability to pursue transactions or development efforts other stockholders may view as beneficial. Further, if Ionis does not continue to own a significant portion of our equity, Ionis' incentive to help us would be diminished. If we fail to achieve the expected benefits of our agreements with Ionis, it may be more difficult, time consuming or expensive for us to develop and commercialize volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development, or may result in our drugs being later to market than those of our competitors or prevent them from ever getting to market. If these events cause delays in new product development we could lose the first in class products in a given therapeutic area.

Risks Related to Our Intellectual Property

If we breach our obligations under our license agreement with Ionis, we could lose our rights to volanesorsen and our other drugs in development.

We obtained our rights to volanesorsen and our other drugs in development under our license agreement with Ionis. If we breach our obligations under this license agreement and, as a result, Ionis subsequently exercises its right to terminate it, we generally would not be able to continue to develop or commercialize volanesorsen, and our other drugs in development that incorporate Ionis' intellectual property, and Ionis would receive a royalty-free, nonexclusive license to our improvements to those programs, meaning we would lose the benefits of our investment in these programs. If we breach our obligations under this license agreement with respect to AKCEA-APO(a)-L$_{Rx}$ or AKCEA-APOCIII-L$_{Rx}$ and, as a result, Ionis exercises its right to terminate it, then our strategic collaboration with Novartis would convert into a direct strategic collaboration between Novartis and Ionis, and Ionis would receive all of the revenue and other benefits associated with that strategic collaboration.

If we cannot protect our patent rights or our other proprietary rights, others may compete more effectively against us.

Our success depends to a significant degree upon whether we can continue to secure and maintain intellectual property rights that protect volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development. However, patents may not issue from any of our pending patent applications in the United States or in other countries and we may not be able to obtain, maintain or enforce our owned or licensed patents and other intellectual property rights which could impact our ability to compete effectively. In addition, the scope of any of our owned or licensed patents may not be sufficiently broad to provide us with a competitive advantage. Furthermore, other parties may successfully challenge, invalidate or circumvent our issued patents or patents licensed to us so that our patent rights do not create an effective competitive barrier or revenue source.

Composition of matter patents on the active pharmaceutical ingredient for a product are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection without regard to any method of use. Our volanesorsen patent portfolio currently includes:

- issued patent claims to the specific antisense sequence and chemical composition of volanesorsen in the United States, Australia, and Europe;
- issued patent claims in the United States and Australia drawn to the use of antisense compounds complementary to an active region of human ApoC-III messenger ribonucleic acid, including the site targeted by volanesorsen;
- additional patent applications designed to protect the volanesorsen composition in Canada; and
- additional methods of use in jurisdictions worldwide for volanesorsen.

The natural term of the issued U.S. patent covering the volanesorsen composition of matter will expire in 2023, but we plan to seek to extend the U.S. patent expiration beyond 2023 based upon the development and regulatory review period in the United States. The natural term of the granted European and Australian patents covering volanesorsen will expire in 2024, but we plan to seek to extend each of these patents beyond 2024 based upon the development and regulatory review periods in Europe and Australia.

We cannot be certain that the U.S. Patent and Trademark Office, or U.S. PTO, and courts in the United States or the patent offices and courts in foreign countries will consider the claims in our owned or licensed patents and applications covering volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development as patentable. Method-of-use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products off-label. Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent, including through legal action.

If we or any licensor partner loses or cannot obtain patent protection for volanesorsen, AKCEA-APO(a)-L$_{Rx}$ or our other drugs in development it could have a material adverse impact on our business.

Intellectual property litigation could cause us to spend substantial resources and prevent us from pursuing our programs.

From time to time we may have to defend our intellectual property rights. If we are involved in an intellectual property dispute, we may need to litigate to defend our rights or assert them against others. Disputes can involve arbitration, litigation or proceedings declared by the U.S. PTO or the International Trade Commission or foreign patent authorities. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios.

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

Our commercial success depends upon our ability and the ability of our strategic partners to develop, manufacture, market and sell our drugs and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. Extensive litigation regarding patents and other intellectual property rights is common in the biotechnology and pharmaceutical industries. We may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our drugs and technology, including interference, derivation, reexamination, post-grant review, opposition, cancellation or similar proceedings before the U.S. PTO or its foreign counterparts. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. We may not be aware of all such intellectual property rights potentially relating to our drugs and their uses. If a third party claims that volanesorsen, AKCEA-APO(a)-L$_{Rx}$, our other drugs in development or our technology infringe its patents or other intellectual property rights, we or our partners may have to discontinue an important product or product line, alter our products and processes, pay license fees or cease certain activities. We may not be able to obtain a license to needed intellectual property on favorable terms, if at all. There are many patents issued or applied for in the biotechnology industry, and we may not be aware of patents or patent applications held by others that relate to our business. This is especially true since patent applications in the United States are filed confidentially for the first 18 months. Moreover, the validity and breadth of biotechnology patents involve complex legal and factual questions for which important legal issues remain. Thus, we do not know with certainty that our drugs or our intended commercialization thereof, does and will not infringe or otherwise violate any third party's intellectual property.

We will not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing, prosecuting and defending patents on drugs in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those we could obtain in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions.

Competitors may use our technologies in jurisdictions where we do not pursue and obtain patent protection to develop their own products. In addition, competitors may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patent rights or other intellectual property rights may not be effective or sufficient to prevent them from competing. Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biotechnology. This could make it difficult for us to stop competitors from infringing our patent rights or misappropriating our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit our right to enforce our patent rights against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. We must ultimately seek patent protection on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

In addition, proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patent rights at risk of being invalidated or interpreted narrowly, could put our owned or licensed patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

If we do not obtain additional protection under the Hatch-Waxman Amendments and similar foreign legislation by extending the patent protection for volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development, our business may be materially harmed.

Depending upon the timing, duration and specifics of the first FDA marketing authorization of volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development, a United States patent that we own or license may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments allow the owner of an approved product to extend patent protection for up to five years as compensation for patent term lost during product development and the FDA regulatory review process. During this period of extension, the scope of protection is limited to the approved product and approved uses.

Although we plan on seeking patent term restoration for our products, we may not succeed if, for example, we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we cannot obtain patent term restoration or the term of any such patent restoration is less than we request, our competitors may enter the market and compete against us sooner than we anticipate, and our ability to generate revenue could be materially adversely affected.

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

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

If we and our partners do not adequately protect the trademarks and trade names for our products, then we and our partners may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our competitors or other third parties may challenge, infringe or circumvent the trademarks or trade names for our products. We and our partners may not be able to protect these trademarks and trade names. In addition, if the trademarks or trade names for one of our products infringe the rights of others, we or our partners may be forced to stop using the trademarks or trade names, which we need for name recognition in our markets of interest. If we cannot establish name recognition based on our trademarks and trade names, we and our partners may not be able to compete effectively and our business may be adversely affected.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

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

- others may make compounds that are similar to our drugs but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we, or our license partners or current or future strategic partners, might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed;
- we, or our license partners or current or future strategic partners, might not have been the first to file patent applications covering our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- our pending licensed patent applications or those that we own in the future may not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

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

Risks Related to Our Business and Industry

We will need to significantly increase the size of our organization, and we may experience difficulties in managing growth.

We are currently a small company. To commercialize volanesorsen, and our other drugs in development that we are responsible for commercializing, we will need to increase our operations and expand our use of third-party contractors. We plan to continue to build our compliance, financial and operating infrastructure to ensure the maintenance of a well-managed company including hiring additional staff within our regulatory, clinical and medical affairs groups and an in-house commercial organization initially focused on marketing and selling volanesorsen, if approved. We currently have limited sales and marketing capability and therefore intend to recruit a specialty sales force in anticipation of volanesorsen's potential approval.

Future growth will impose significant added responsibilities on our management, including the need to identify, recruit, maintain and integrate additional employees. In addition, to meet our obligations as a public company, we will need to increase our general and administrative capabilities. Our current management, personnel and systems may not be adequate to support this future growth. Our future financial performance and our ability to commercialize our drugs and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to:

- manage our clinical studies and the regulatory process effectively;
- manage the manufacturing of our drugs for clinical and commercial use;
- integrate current and additional management, administrative, financial and sales and marketing personnel;
- develop a marketing and sales infrastructure;
- hire new personnel necessary to effectively commercialize volanesorsen and our other drugs in development;
- develop our administrative, accounting and management information systems and controls; and
- hire and train additional qualified personnel.

Our staff, financial resources, systems, procedures or controls may be inadequate to support our operations and our management may be unable to successfully manage future market opportunities or our relationships with customers and other third parties.

If we do not progress in our programs as anticipated, the price of our securities could decrease.

For planning purposes, we estimate and may disclose the timing of a variety of clinical, regulatory and other milestones, such as when we anticipate a certain drug will enter the clinic, when we anticipate completing a clinical study, when we anticipate filing an application for marketing authorization, or when we or our partners plan to commercially launch a drug. We base our estimates on present facts and a variety of assumptions. Many underlying assumptions are outside of our control. If we do not achieve milestones in accordance with our or our investors' or securities analysts' expectations, including milestones related to volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development, the price of our securities could decrease.

The loss of key personnel, or if we cannot attract and retain highly skilled personnel, could make it more difficult to run our business and reduce our likelihood of success.

We are dependent on the principal members of our management and scientific staff. We do not have employment agreements with any of our executive officers that would prevent them from leaving us. The loss of management and key scientific employees might slow the achievement of important research and development goals. It is also critical to our success that we recruit and retain qualified scientific personnel to perform development work and marketing, sales and commercial support personnel to perform commercialization activities. We may not be able to attract and retain skilled and experienced scientific and commercial personnel on acceptable terms because of intense competition for experienced personnel among many pharmaceutical and health care companies, universities and non-profit research institutions. In addition, failure to successfully complete clinical studies, obtain regulatory approvals or effectively commercialize drugs may make it more challenging to recruit and retain qualified personnel.

We are exposed to potential product liability claims, and insurance against these claims may not be available to us at a reasonable rate in the future or at all.

Our business exposes us to potential product liability risks that are inherent in the testing, manufacturing, marketing and sale of therapeutic products, including potential product liability claims related to volanesorsen, AKCEA-APO(a)-L$_{Rx}$ and our other drugs in development. We have clinical study insurance coverage and commercial product liability insurance coverage. In addition, Novartis has agreed to indemnify us against specific claims arising from Novartis' development and commercialization of AKCEA-APO(a)-L$_{Rx}$ and AKCEA-APOCIII-L$_{Rx}$. However, this insurance coverage and indemnities may not be adequate to cover claims against us. Insurance may not be available to us at an acceptable cost, if at all. Regardless of their merit or eventual outcome, products liability claims may result in decreased demand for our drug products, injury to our reputation, withdrawal of clinical study volunteers and loss of revenue. Thus, whether or not we are insured or indemnified, a product liability claim or product recall may result in losses that could be material.

Because we use biological materials, hazardous materials, chemicals and radioactive compounds, if we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected.

Our development and manufacturing activities involve the use of potentially harmful biological materials as well as materials, chemicals and various radioactive compounds that could be hazardous to human health and safety or the environment. We cannot completely eliminate the risk of contamination, which could cause:

- interruption of our development, manufacturing and distribution efforts;
- injury to our employees and others;
- environmental damage resulting in costly clean up; and
- liabilities under federal, state and local laws and regulations governing health and human safety, as well as the use, storage, handling and disposal of these materials and resultant waste products.

In such an event, we may be held liable for any resulting damages, and any liability could exceed our resources. Although we carry insurance in amounts and types that we consider commercially reasonable, we do not have insurance coverage for losses relating to an interruption of our development, manufacturing or commercialization efforts caused by contamination, and the coverage or coverage limits of our insurance policies may not be adequate. If our losses exceed our insurance coverage, our financial condition would be adversely affected.

A variety of risks associated with operating our business and, following approval, marketing our drugs internationally could materially adversely affect our business.

In addition to our U.S. operations, we plan to establish operations and, following approval, commercialize our products in Europe and other countries globally. We face risks associated with our current and planned international operations, including possible unfavorable regulatory, pricing and reimbursement, political, tax and labor conditions, which could harm our business. Once we establish international operations we will be subject to numerous risks associated with international business activities, including:

- compliance with differing or unexpected regulatory requirements for our drugs and foreign employees;
- complexities associated with managing multiple payor reimbursement regimes, government payors or patient self-pay systems;
- difficulties in staffing and managing foreign operations;
- in certain circumstances, increased dependence on the commercialization efforts and regulatory compliance of third-party distributors or strategic partners;
- foreign government taxes, regulations and permit requirements;
- U.S. and foreign government tariffs, trade restrictions, price and exchange controls and other regulatory requirements;
- anti-corruption laws, including the Foreign Corrupt Practices Act, or the FCPA, and its equivalent in foreign jurisdictions;
- economic weakness, including inflation, natural disasters, war, events of terrorism or political instability in particular foreign countries;
- fluctuations in currency exchange rates, which could result in increased operating expenses and reduced revenue, and other obligations related to doing business in another country;
- compliance with tax, employment, privacy, immigration and labor laws, regulations and restrictions for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the United States; and
- changes in diplomatic and trade relationships.

The UK's anticipated exit from the European Union could increase these risks.

Our business activities outside of the United States are subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate, including the U.K.'s Bribery Act 2010. In many other countries, the healthcare providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, any dealings with these prescribers and purchasers may be subject to regulation under the FCPA. There is no certainty that all employees and third-party business partners (including our distributors, wholesalers, agents, contractors and other partners) will comply with anti-bribery laws. In particular, we do not control the actions of manufacturers and other third-party agents, although we may be liable for their actions. Violation of these laws may result in civil or criminal sanctions, which could include monetary fines, criminal penalties, and disgorgement of past profits, which could have a material adverse impact on our business and financial condition.

If a natural or man-made disaster strikes our development or manufacturing facilities or otherwise affects our business, it could delay our progress developing and commercializing our drugs.

We currently rely on Ionis to manufacture our clinical supplies in a manufacturing facility located in Carlsbad, California. The facilities and the equipment required to develop and manufacture our drugs would be costly to replace and could require substantial lead time to repair or replace. Natural or man-made disasters, including, without limitation, earthquakes, floods, fires and acts of terrorism may harm these facilities. If a disaster affects these facilities, our and our partners' development and commercialization efforts would be delayed. Although we possess insurance for damage to our property and the disruption of our business from casualties, this insurance may not be sufficient to cover all of our potential losses and may not continue to be available to us on acceptable terms, or at all. In addition, a shutdown of the U.S. government, including the FDA could harm or delay our development and commercialization activities.

Our business and operations would suffer in the event of computer system failures.

Despite the implementation of security measures, our internal computer systems, and those of our CROs, manufacturers and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If issues were to arise and cause interruptions in our operations, it could result in a material disruption of our drug programs. For example, the loss of clinical study data from completed or ongoing or planned clinical studies could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of volanesorsen, AKCEA-APO(a)-L_{Rx} and our other drugs in development could be delayed.

Risks Related to Our Common Stock

We are an "emerging growth company" and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies, our common stock may be less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act, and we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies" including, but not limited to, the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We cannot predict if investors will find our common stock less attractive if we choose to rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

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

Prior to the completion of our IPO in July 2017, no public market for our common stock existed. An active public trading market for our common stock may not be sustained. The lack of an active market may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. The lack of an active market may also reduce the fair value of your shares. An inactive market may also impair our ability to raise capital to continue to fund operations by selling shares.

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

Fluctuations in the price of our common stock could contribute to the loss of all or part of your investment. There has been a public market for our common stock for a limited period of time. The trading price of our common stock is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. Any of the factors listed below could have a material adverse effect on your investment in our common stock and our common stock may trade at prices significantly below your purchase price. In such circumstances the trading price of our common stock may not recover and may experience a further decline.

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

- our failure to effectively develop and commercialize volanesorsen and our other drugs in development;
- Novartis' failure to exercise its option and/or effectively develop and commercialize AKCEA-APO(a)-L_{Rx} and AKCEA-APOCIII-L_{Rx} to the extent it exercises its option to license those drugs from us;
- changes in the market's expectations about our operating results;
- adverse results or delays in preclinical or clinical studies;

- our decision to initiate a clinical study, not to initiate a clinical study or to terminate an existing clinical study;
- adverse regulatory decisions, including failure to receive regulatory approval for volanesorsen, AKCEA-APO(a)-L_{Rx} and our other drugs in development;
- success or failure of competitive products or antisense drugs more generally;
- adverse developments concerning our manufacturers or our strategic partnerships;
- inability to obtain adequate product supply for any drug for clinical studies or commercial sale or inability to do so at acceptable prices;
- the termination of a strategic partnership or the inability to establish additional strategic partnerships;
- unanticipated serious safety concerns related to the use of volanesorsen, AKCEA-APO(a)-L_{Rx} and our other drugs in development;
- adverse safety or other clinical results, such as those that have occurred in the past or that may occur in the future, related to drugs being developed by Ionis or other companies that are or may be perceived to be similar to our drugs;
- our ability to effectively manage our growth;
- the size and growth, if any, of the targeted market;
- our operating results do not meet the expectation of securities analysts or investors in a particular period;
- actual or anticipated fluctuations in our quarterly financial results or the quarterly financial results of companies perceived to be similar to us;
- securities analysts do not publish reports about us or our business or publish negative reports;
- changes in financial estimates and recommendations by securities analysts concerning our company, our market opportunity, or the biotechnology and pharmaceutical industries in general;
- operating and stock price performance of other companies that investors deem comparable to us;
- overall performance of the equity markets;
- announcements by us or our competitors of acquisitions, new drugs or programs, significant contracts, commercial relationships or capital commitments;
- our and our strategic partners' ability to successfully market volanesorsen, AKCEA-APO(a)-L_{Rx} and our other drugs in development;
- changes in laws and regulations affecting our business, including but not limited to clinical study requirements for approvals;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain and maintain patent protection for volanesorsen, AKCEA-APO(a)-L_{Rx} and our other drugs in development;
- commencement of, or involvement in, litigation involving our company, our general industry, or both;
- changes in our capital structure, such as future issuances of securities or the incurrence of additional debt;
- the volume of shares of our common stock available for public sale;
- additions or departures of key scientific or management personnel;
- any major change in our board or management;
- changes in accounting practices;
- ineffectiveness of our internal control over financial reporting;
- significant changes in our relationship with Ionis;
- sales of substantial amounts of common stock by our directors, executive officers or significant stockholders or the perception that such sales could occur; and
- general economic and political conditions such as recessions, interest rates, fuel prices, elections, drug pricing policies, international currency fluctuations and acts of war or terrorism.

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

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

Sales of our common stock in the public market, or the perception that these sales may occur, could cause the market price of our common stock to decline. Immediately following our IPO and concurrent private placement we had 66,541,629 shares of common stock outstanding. Of these, only 14,843,750 shares of our common stock sold in our IPO are freely transferable without restriction or additional registration under the Securities Act. Novartis has agreed that it will not sell any of the shares it purchased in the concurrent private placement until the earlier of January 5, 2020 or six months after we stop developing a drug under our agreement with Novartis. Thereafter, Novartis may only sell a limited number of shares each day. The remaining shares outstanding after the IPO will be available for sale, upon the expiration of the lock-up period on January 15, 2018, subject to volume and other restrictions as applicable under Rule 144 under the Securities Act. At its discretion, Cowen and Company, LLC may release any or all of these shares prior to expiration of the lock-up period. Immediately after the lock-up agreements expire, up to an additional 45,447,879 shares of common stock held by Ionis will be eligible for sale in the public market, all of which will be subject to volume limitations under Rule 144 under the Securities Act. In addition, 9,000,000 shares of common stock that are either subject to outstanding options or reserved for future issuance under our employee benefit plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act. To the extent the holders of these shares sell them into the market or our stockholders believe these sales might occur, the market price of our common stock could decline.

We cannot predict with certainty whether or when Ionis will sell a substantial number of shares of our common stock. Ionis' sale of a substantial number of shares, or a perception that such sales could occur, could significantly reduce the market price of our common stock.

We do not expect to pay any cash dividends for the foreseeable future.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any cash dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our operations. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

Our ability to use our net operating loss carryovers and certain other tax attributes may be limited.

As described above, we have incurred net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future. Under the Internal Revenue Code of 1986, as amended, or the Code, a corporation is generally allowed a deduction for net operating losses, or NOLs, carried over from a prior taxable year. Under that provision, we can carry forward our NOLs to offset our future taxable income, if any, until such NOLs are used or expire. The same is true of other unused tax attributes, such as tax credits.

If a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, Sections 382 and 383 of the Code limit the corporation's ability to use carryovers of its pre-change NOLs, credits and certain other tax attributes to reduce its tax liability for periods after the ownership change. Our issuance of common stock pursuant to our IPO may result in a limitation under Sections 382 and 383, either separately or in combination with certain prior or subsequent shifts in the ownership of our common stock. As a result, our ability to use carryovers of our pre-change NOLs and credits to reduce our future U.S. federal income tax liability may be subject to limitations. This could result in increased U.S. federal income tax liability for us if we generate taxable income in a future period. Limitations on the use of NOLs and other tax attributes could also increase our state tax liability. The use of our tax attributes will also be limited to the extent that we do not generate positive taxable income in future tax periods.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

Provisions in our amended and restated certificate of incorporation, our amended and restated bylaws and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation, amended and restated bylaws and Delaware law contain provisions that may have the effect of delaying or preventing a change in control of us or changes in our management. Our amended and restated certificate of incorporation and bylaws include provisions that:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- specify that only board of directors or holders of greater than 10% of our common stock can call special meetings of our stockholders;
- prohibit stockholder action by written consent once Ionis no longer holds a majority of our voting power;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that a majority of directors then in office, even though less than a quorum, may fill vacancies on our board of directors;
- specify that no stockholder is permitted to cumulate votes at any election of directors;
- expressly authorize our board of directors to modify, alter or repeal our amended and restated bylaws; and
- require supermajority votes of the holders of our common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated bylaws.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management. Further, Novartis has agreed that until Novartis holds less than 7.5% of our outstanding common stock, Novartis will vote the Novartis Private Placement Shares consistent with the recommendation of our board of directors. Although Novartis has retained the right to vote the Novartis Private Placement Shares in its sole discretion in connection with certain enumerated matters, including any transaction which would result in our change of control, our agreement with Novartis may nevertheless delay or prevent changes in our management or board of directors.

In addition, because we are incorporated in the State of Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us.

Any provision of our amended and restated certificate of incorporation or amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit your opportunity to receive a premium for your shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Our bylaws designate the Court of Chancery of the State of Delaware and federal court within the State of Delaware as the exclusive forum for certain types of actions and proceedings that our stockholders may initiate, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our bylaws provide that, subject to limited exceptions, the Court of Chancery of the State of Delaware and federal court within the State of Delaware will be exclusive forums for any:

- derivative action or proceeding brought on our behalf;
- action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders;
- action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws; or
- other action asserting a claim against us that is governed by the internal affairs doctrine.

Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our bylaws described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find these provisions of our amended and restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to changes in interest rates primarily from our investments in certain short-term investments. We place our cash equivalents and short-term investments with reputable financial institutions. We primarily invest our excess cash in commercial paper and debt instruments of the U.S. Treasury, financial institutions, corporations, and U.S. government agencies with strong credit ratings and an investment grade rating at or above A-1, P-1 or F-1 by Moody's, Standard & Poor's, or Fitch, respectively. We have established guidelines relative to diversification and maturities that are designed to maintain safety and liquidity. We periodically review and modify these guidelines to maximize trends in yields and interest rates without compromising safety and liquidity. We typically hold our investments for the duration of the term of the respective instrument. We do not utilize derivative financial instruments, derivative commodity instruments or other market risk sensitive instruments, positions or transactions to manage exposure to interest rate changes. Accordingly, we believe that, while the securities we hold are subject to changes in the financial standing of the issuer of such securities, we are not subject to any material risks arising from changes in interest rates, foreign currency exchange rates, commodity prices, equity prices or other market changes that affect market risk sensitive instruments.

Our results of operations are subject to foreign currency exchange rate fluctuations as we have a foreign subsidiary, Akcea Therapeutics UK Ltd., or Akcea UK., with a functional currency other than the U.S. dollar. We created Akcea UK to support our initial pre-commercialization activities in Europe, and to serve as a potential entity for future United Kingdom and/or European operations. We translate Akcea UK's functional currency, the British pound sterling, or British pound, to our reporting currency the U.S. dollar. As a result, our financial position, results of operations and cash flows can be affected by market fluctuations in the British pound to U.S. dollar exchange rate which are difficult to predict. However, because Akcea UK currently has limited operations, the effect on fluctuations of the British pound to U.S. dollar exchange rate on our consolidated results is immaterial to our consolidated financial statements. Our business strategy incorporates potentially significant international expansion, particularly in anticipation of approval of volanesorsen, therefore we expect that the impact of foreign currency exchange rate fluctuations may become more substantial in the future.

ITEM 4. CONTROLS AND PROCEDURES

We maintain disclosure controls and procedures that are designed to ensure that information we are required to disclose in our Exchange Act reports is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. We design and evaluate our disclosure controls and procedures recognizing that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance and not absolute assurance of achieving the desired control objectives.

As of our most recently completed fiscal year and as of the end of the period covered by this Quarterly Report on Form 10-Q, we carried out an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer. Based on our evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of June 30, 2017. There have been no significant changes in our internal controls or in other factors that could significantly affect internal controls subsequent to June 30, 2017.

We also performed an evaluation of any change in our internal control over financial reporting that occurred during our last fiscal quarter and that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting. We conducted this evaluation under the supervision of and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer. That evaluation did not identify any change in our internal control over financial reporting that occurred during our latest fiscal quarter and 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

Not applicable.

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

(a) Recent Sales of Unregistered Equity Securities

From April 1, 2017 through June 30, 2017, pursuant the terms of our 2015 Equity Incentive Plan, we granted to our employees and directors stock option awards to purchase up to an aggregate of 1,678,661 shares of our common stock, at an exercise price of $12.21 per share. The offers, sales and issuances of these securities were deemed to be exempt from registration under Rule 701 promulgated under the Securities Act, or Rule 701, in that the transactions were by an issuer not involving any public offering or under Section 4(a)(2) of the Securities Act or under compensatory benefit plans and contracts relating to compensation as provided under Rule 701. The recipients of such securities were our employees, directors or consultants and received the securities under our equity incentive plans. Appropriate legends were affixed to the securities issued in these transactions.

(b) Use of Proceeds

On July 19, 2017, we closed our initial public offering of 17,968,750 shares of common stock at an offering price of $8.00 per share, resulting in gross proceeds to us of approximately $143.8 million. All of the shares issued and sold in our initial public offering were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-216949), which was declared effective by the SEC on July 13, 2017. Cowen and Company, LLC, Stifel, Nicolaus & Company, Incorporated and Wells Fargo Securities, LLC acted as joint book-running managers for our initial public offering and BMO Capital Markets Corp. acted as lead manager for our initial public offering. The offering commenced on June 20, 2017 and did not terminate before all of the securities registered in the registration statement were sold.

The net proceeds to us, after deducting underwriting discounts and commissions of approximately $8.4 million and offering expenses of approximately $3.0 million, were approximately $132.4 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning ten percent or more of any class of our equity securities or to any other affiliates. There has been no material change in the planned use of proceeds from our initial public offering from those disclosed in the final prospectus for our initial public offering dated as of on July 13, 2017 and filed with the SEC pursuant to Rule 424(b)(4).

As of June 30, 2017, $0.5 million of expenses incurred in connection with our initial public offering had not yet been paid.

(c) Issuer Purchase of Equity Securities

None.

ITEM 3. DEFAULT UPON SENIOR SECURITIES

None.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

ITEM 5. OTHER INFORMATION

Not Applicable.

ITEM 6. EXHIBITS

a. Exhibits

Exhibit Number	Description of Document
3.1	Amended and Restated Certificate of Incorporation of Akcea Therapeutics, Inc.- Filed as an exhibit to the Registrant's Current Report on Form 8-K (File No. 001-38137), filed with the Securities and Exchange Commission on July 19, 2017, and incorporated herein by reference.
3.2	Amended and Restated Bylaws of Akcea Therapeutics, Inc.- Filed as an exhibit to the Registrant's Current Report on Form 8-K (File No. 001-38137), filed with the Securities and Exchange Commission on July 19, 2017, and incorporated herein by reference.
31.1	Certification by Chief Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as amended.
31.2	Certification by Chief Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as amended.
32.1*	Certification Pursuant to 18 U.S.C. Section 1350 as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101	The following financial statements from the Akcea Therapeutics, Inc. Quarterly Report on Form 10-Q for the quarter ended June 30, 2017, formatted in Extensive Business Reporting Language (XBRL): (i) condensed consolidated balance sheets, (ii) condensed consolidated statements of operations, (iii) condensed consolidated statements of comprehensive loss, (iv) condensed consolidated statements of cash flows and (v) notes to condensed consolidated financial statements (detail tagged).

* This certification is deemed not filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, this Report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Signatures	Title	Date
/s/ PAULA SOTEROPOULOS Paula Soteropoulos	President and Chief Executive Officer (Principal executive officer)	August 8, 2017
/s/ ELIZABETH L. HOUGEN Elizabeth L. Hougen	Chief Financial Officer (Principal financial and accounting officer)	August 8, 2017

EXHIBIT 31.1

CERTIFICATION

I, Paula Soteropoulos, certify that:

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

2. Based on my knowledge, this quarterly 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 quarterly report;

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

Dated: August 8, 2017

/s/ PAULA SOTEROPOULOS

Paula Soteropoulos
President and Chief Executive Officer

EXHIBIT 31.2

CERTIFICATION

I, Elizabeth L. Hougen, certify that:

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

2. Based on my knowledge, this quarterly 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 quarterly report;

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

Dated: August 8, 2017

/s/ ELIZABETH L. HOUGEN

Elizabeth L. Hougen
Chief Financial Officer

Exhibit 32.1

CERTIFICATION

Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, Paula Soteropoulos, the President and Chief Executive Officer of Akcea Therapeutics, Inc., (the "Company"), and Elizabeth L. Hougen, the Chief Financial Officer of the Company, each hereby certifies that, to the best of his or her knowledge:

1. The Company's Quarterly Report on Form 10-Q for the period ended June 30, 2017, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934, as amended; and

2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition of the Company at the end of the period covered by the Periodic Report and the results of operations of the Company for the period covered by the Periodic Report.

Dated: August 8, 2017

/s/ PAULA SOTEROPOULOS	/s/ ELIZABETH L. HOUGEN
Paula Soteropoulos President and Chief Executive Officer	Elizabeth L. Hougen Chief Financial Officer

A signed original of this written statement required by Section 906 has been provided to Akcea Therapeutics, Inc. and will be retained by Akcea Therapeutics, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.