DICERNA PHARMACEUTICALS INC

FORM 10-Q
(Quarterly Report)

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

Form 10-Q

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

For the quarterly period ended September 30, 2017

OR

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

For the transition period from _____to _____

Commission File Number: 001-36281

DICERNA PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**20-5993609**
(State or other jurisdiction of incorporation or organization)	**(IRS Employer Identification No.)**

87 Cambridgepark Drive
Cambridge, MA 02140
(Address of principal executive offices and zip code)

(617) 621-8097
(Registrant's telephone number, including area code)

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

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

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

Large accelerated filer	☐	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 12b-2 of the Exchange Act) Yes ☐ No ☒

As of November 1, 2017, there were 20,848,503 shares of the registrant's common stock, par value $0.0001 per share, outstanding.

DICERNA PHARMACEUTICALS, INC.
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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q includes "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements other than statements of historical fact are "forward-looking statements" for purposes of this Quarterly Report on Form 10-Q. In some cases, you can identify forward-looking statements by terminology such as "may," "could," "will," "would," "should," "expect," "plan," "anticipate," "believe," "estimate," "intend," "predict," "seek," "contemplate," "project," "continue," "potential," "ongoing," "goal," or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- how long we expect to maintain liquidity to fund our planned level of operations and our ability to obtain additional funds for our operations;
- the initiation, timing, progress and results of our research and development programs, preclinical studies, any clinical trials and Investigational New Drug ("IND") application, Clinical Trial Application ("CTA"), New Drug Application ("NDA") and other regulatory submissions;
- our ability to identify and develop product candidates for treatment of additional disease indications;
- our or a collaborator's ability to obtain and maintain regulatory approval of any of our product candidates;
- the rate and degree of market acceptance of any approved product candidates;
- the commercialization of any approved product candidates;
- our ability to establish and maintain additional collaborations and retain commercial rights for our product candidates in the collaborations;
- the implementation of our business model and strategic plans for our business, technologies and product candidates;
- our estimates of our expenses, ongoing losses, future revenue and capital requirements;
- our ability to obtain and maintain intellectual property protection for our technologies and product candidates and our ability to operate our business without infringing the intellectual property rights of others;
- our reliance on third parties to conduct our preclinical studies or any future clinical trials;
- our reliance on third party supply and manufacturing partners to supply the materials and components for, and manufacture, our research and development, preclinical and clinical trial drug supplies;
- our ability to attract and retain qualified key management and technical personnel;
- our dependence on our existing collaborators, Boehringer Ingelheim International GmbH ("BI") and Kyowa Hakko Kirin Co., Ltd. ("KHK"), for developing, obtaining regulatory approval for and commercializing product candidates in the collaboration;
- our receipt and timing of any milestone payments or royalties under our research collaboration and license agreement with KHK or any future arrangements with any other collaborators;
- our expectations regarding the time during which we will be an emerging growth company under the Jumpstart Our Business Startups Act;
- our financial performance; and
- developments relating to our competitors or our industry.

These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those set forth in Part II, Item 1A—"Risk Factors" below and for the reasons described elsewhere in this Quarterly Report on Form 10-Q. Any forward-looking statement in this Quarterly Report on Form 10-Q reflects our current view with respect to future events and is subject to these and other risks, uncertainties and assumptions relating to our operations, results of operations, industry and future growth. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Quarterly Report on Form 10-Q also contains estimates, projections and other information concerning our industry, our business and the markets for certain drugs, including data regarding the estimated size of those markets, their projected growth rates and the incidence of certain medical conditions. Information that is based on estimates, forecasts, projections or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained these industry, business, market and other data from reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources. In some cases, we do not expressly refer to the sources from which these data are derived.

Except where the context otherwise requires, in this Quarterly Report on Form 10-Q, "we," "us," "our," "Dicerna" and the "Company" refer to Dicerna Pharmaceuticals, Inc. and, where appropriate, its consolidated subsidiaries.

Trademarks

This Quarterly Report on Form 10-Q includes trademarks, service marks and trade names owned by us or by other companies. All trademarks, service marks and trade names included in this Quarterly Report on Form 10-Q are the property of their respective owners.

PART I. FINANCIAL INFORMATION

Item 1. Financial Statements

DICERNA PHARMACEUTICALS, INC.
Condensed Consolidated Balance Sheets
(Unaudited)
(In thousands, except share data and par value)

	September 30, 2017	December 31, 2016
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 30,960	$ 20,865
Held-to-maturity investments (Note 3)	44,959	25,009
Prepaid expenses and other current assets	3,915	1,952
Total current assets	79,834	47,826
NONCURRENT ASSETS:		
Property and equipment—net	1,704	2,234
Restricted cash equivalents	1,116	1,116
Other noncurrent assets	72	76
Total noncurrent assets	2,892	3,426
TOTAL ASSETS	$ 82,726	$ 51,252
LIABILITIES AND STOCKHOLDERS' EQUITY		
CURRENT LIABILITIES:		
Accounts payable	$ 5,392	$ 4,318
Accrued expenses and other current liabilities	5,130	5,726
Total current liabilities	10,522	10,044
TOTAL LIABILITIES	10,522	10,044
Commitments and contingencies (Note 7)		
PREFERRED STOCK, $0.0001 par value and 5,000,000 shares authorized:		
Redeemable convertible preferred stock—740,126 and no shares issued and outstanding at September 30, 2017 and December 31, 2016, respectively (aggregate liquidation preference of $74,014 and $0 at September 30, 2017 and December 31, 2016, respectively) (Note 4)	75,983	—
STOCKHOLDERS' (DEFICIT) EQUITY:		
Common stock, $0.0001 par value—150,000,000 shares authorized at September 30, 2017 and December 31, 2016; 20,847,754 shares and 20,753,001 shares issued and outstanding at September 30, 2017 and December 31, 2016, respectively	2	2
Additional paid-in capital	296,434	296,962
Accumulated deficit	(300,215)	(255,756)
Total stockholders' (deficit) equity	(3,779)	41,208
TOTAL LIABILITIES AND STOCKHOLDERS' (DEFICIT) EQUITY	$ 82,726	$ 51,252

The accompanying notes are an integral part of these condensed consolidated financial statements.

DICERNA PHARMACEUTICALS, INC.
Condensed Consolidated Statements of Operations
(Unaudited)
(In thousands, except share and per share data)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2017	2016	2017	2016
Revenue	$ 474	$ 162	$ 859	$ 162
Operating expenses:				
Research and development	9,001	10,061	27,197	32,357
General and administrative	6,685	4,338	18,481	13,478
Total operating expenses	15,686	14,399	45,678	45,835
Loss from operations	(15,212)	(14,237)	(44,819)	(45,673)
Interest income	179	61	360	182
Net loss	(15,033)	(14,176)	(44,459)	(45,491)
Dividends on redeemable convertible preferred stock	(4,111)	—	(6,733)	—
Deemed dividend related to beneficial conversion feature of redeemable convertible preferred stock	—	—	(6,144)	—
Net loss attributable to common stockholders	$ (19,144)	$ (14,176)	$ (57,336)	$ (45,491)
Net loss per share attributable to common stockholders—basic and diluted	$ (0.92)	$ (0.68)	$ (2.76)	$ (2.20)
Weighted average common shares outstanding—basic and diluted	20,841,728	20,752,416	20,809,372	20,708,600

The accompanying notes are an integral part of these condensed consolidated financial statements.

DICERNA PHARMACEUTICALS, INC.
Condensed Consolidated Statements of Cash Flows
(Unaudited)
(In thousands)

	Nine Months Ended September 30,	
	2017	2016
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (44,459)	$ (45,491)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	6,003	7,067
Depreciation and amortization	571	627
Net amortization of premium/discount on investments	(106)	65
Loss on disposal of property and equipment	51	—
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	(1,963)	(300)
Accounts payable	1,114	983
Accrued expenses and other liabilities	(588)	(108)
Deferred rent	4	—
Net cash used in operating activities	(39,373)	(37,157)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of property and equipment	(133)	(375)
Maturities of held-to-maturity investments	45,000	33,500
Purchases of held-to-maturity investments	(64,853)	(20,016)
Net cash (used in) provided by investing activities	(19,986)	13,109
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	70,000	—
Redeemable convertible preferred stock issuance costs	(750)	—
Proceeds from stock option exercises and issuances under employee stock purchase plan	215	561
Settlement of restricted stock for tax withholding	(11)	(27)
Net cash provided by financing activities	69,454	534
INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS	10,095	(23,514)
CASH AND CASH EQUIVALENTS — Beginning of period	20,865	56,058
CASH AND CASH EQUIVALENTS — End of period	$ 30,960	$ 32,544
SUPPLEMENTAL CASH FLOW INFORMATION:		
NONCASH FINANCING ACTIVITIES:		
Dividends on redeemable convertible preferred stock	$ 6,733	$ —
Deemed dividend related to beneficial conversion feature of redeemable convertible preferred stock	$ 6,144	$ —
NONCASH INVESTING ACTIVITIES:		
Property and equipment purchases included in accounts payable	$ —	$ 52

The accompanying notes are an integral part of these condensed consolidated financial statements.

DICERNA PHARMACEUTICALS, INC.
Notes to Condensed Consolidated Financial Statements
(Unaudited)
(tabular amounts in thousands, except share and per share data and where otherwise noted)

1. Description of Business and Basis of Presentation

Business

Dicerna Pharmaceuticals, Inc. ("Dicerna" or the "Company"), a Delaware corporation founded in 2006 and located in Cambridge, Massachusetts, is a biopharmaceutical company focused on the discovery and development of innovative subcutaneously delivered ribonucleic acid interference ("RNAi")-based pharmaceuticals using its GalXC ™ RNAi platform for the treatment of diseases involving the liver, including rare diseases, chronic liver diseases, cardiovascular diseases and viral infectious diseases.

Basis of presentation

These condensed consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP") and in accordance with the rules and regulations of the Securities and Exchange Commission ("SEC") for interim financial information. Accordingly, these condensed consolidated financial statements do not include all of the information and notes required by GAAP to constitute a complete set of financial statements. These condensed consolidated financial statements have been prepared on the same basis as the Company's annual consolidated financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary to present fairly the Company's financial position at September 30, 2017 and results of operations and cash flows for the interim periods ended September 30, 2017 and 2016. These unaudited condensed consolidated interim financial statements should be read in conjunction with the Company's audited consolidated financial statements and notes thereto included in the Company's Annual Report on Form 10-K for the year ended December 31, 2016, as amended. The results of the three and nine months ended September 30, 2017 are not necessarily indicative of the results to be expected for the year ending December 31, 2017 or for any other interim period or for any other future year.

Significant judgments and estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the revenue and expenses incurred during the reporting periods. On an ongoing basis, the Company evaluates judgments and estimates, including those related to accrued expenses, stock-based compensation and in relation to the accounting for, including cumulative dividends on, the Redeemable Convertible Preferred, as defined below. The Company bases its estimates on historical experience and on various other factors that the Company believes are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results could differ materially from those estimates.

Liquidity risk

Based on the Company's current operating plan and liquidity, including the receipt of gross proceeds of $70.0 million from the issuance of the Company's Redeemable Convertible Preferred, as defined below, on April 11, 2017 (see Note 4) and the receipt of upfront proceeds in connection with the BI Agreement, defined and discussed in Note 8, management believes that available cash, cash equivalents and held-to-maturity investments will be sufficient to fund the Company's planned level of operations for at least the 12-month period following November 2, 2017, which is the date that these condensed consolidated financial statements have been issued. Notwithstanding the availability of current liquidity, the Company's ability to fund its planned preclinical and clinical operations, including completion of its planned clinical trials, will depend on its ability to raise additional capital through a combination of public or private equity offerings, debt financings, and research collaborations and license agreements. If the Company is unable to generate funding from one or more of these sources within a reasonable timeframe, it may have to delay, reduce or terminate its research and development programs, preclinical or clinical trials, limit strategic opportunities or undergo reductions in its workforce or other corporate restructuring activities.

Summary of Significant Accounting Policies — There have been no changes to the significant accounting policies disclosed in the Company's most recent Annual Report on Form 10-K, as amended, except as required by recently adopted accounting pronouncements, as discussed below, and as related to the Redeemable Convertible Preferred, as defined below.

Recent Accounting Pronouncements

Adopted in 2017

Stock-based compensation

In March 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2016-09, *Compensation—Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting* ("ASU 2016-09"), which involves several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities and classification in the statement of cash flows. Also under the new guidance, excess tax benefits and deficiencies are to be recognized as income tax expense or benefit in the income statement as discrete items in the reporting period in which they occur instead of an increase or decrease to stockholders' equity. With regard to forfeitures, an entity may make an accounting policy election either to estimate the number of awards that are expected to vest or account for forfeitures when they occur. The Company adopted ASU 2016-09 on January 1, 2017, and as a result, it will track stock option deductions in its net operating loss deferred tax asset on a modified retrospective basis. In addition, the Company's policy has been to estimate forfeitures as of the grant date. The Company will continue to maintain its policy to estimate forfeiture as of the grant date in the future. Since the Company historically has maintained a full valuation allowance on its net deferred tax asset, there is no net impact to the Company's accumulated deficit or on its net loss per share attributable to common stockholders from the adoption of ASU 2016-09. As such, adoption of this guidance did not have any impact on the Company's consolidated financial statements.

Not yet adopted

Revenue recognition

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers (Topic 606),* which amends the guidance for accounting for revenue from contracts with customers, superseding the revenue recognition requirements in Accounting Standards Codification Topic 605, *Revenue Recognition* , and creates a new Topic 606, *Revenue from Contracts with Customers* ("Topic 606"). Topic 606 is effective for annual reporting periods beginning after December 15, 2017, with early adoption permitted. Per Topic 606, two adoption methods are allowed: retrospectively to all prior reporting periods presented, with certain practical expedients permitted, or retrospectively with the cumulative effect of initially adopting Topic 606 recognized at the date of initial application. The Company has not yet determined which adoption method will be utilized or the effect that adoption of Topic 606 may have on the Company's consolidated financial statements. However, management has determined that the new guidance will be applied only to contracts that are not completed as of January 1, 2018, as allowed by Topic 606. Additionally, management has determined that income associated with the Company's National Institutes of Health ("NIH") grant does not meet the definition of revenue under Topic 606 and that, while there will be no cumulative effect on initial adoption of Topic 606 related to the Company's grants, grant income will no longer be presented as revenue in the Company's consolidated statement of operations.

Income taxes

In October 2016, the FASB issued ASU No. 2016-16, *Accounting for Income Taxes: Intra-Entity Asset Transfers of Assets Other than Inventory* ("ASU 2016-16"), which is part of the FASB's simplification initiative aimed at reducing complexity in accounting standards. ASU 2016-16 eliminates the current exception that the tax effects of intra-entity asset transfers (intercompany sales) be deferred until the transferred asset is sold to a third party or otherwise recovered through use. Instead, the new guidance will require a reporting entity to recognize any tax expense from the sale of the asset in the seller's tax jurisdiction when the transfer occurs, even though the pre-tax effects of that transaction are eliminated in consolidation. Any deferred tax asset that arises in the buyer's jurisdiction would also be recognized at the time of the transfer. ASU 2016-16 will be effective for public business entities in fiscal years beginning after December 15, 2017, including interim periods within those years. Management is currently evaluating the potential impact that this guidance may have on the Company's consolidated financial statements.

Leases

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)* ("ASU 2016-02"), which amends the existing accounting standards for lease accounting, including requiring lessees to recognize most leases on their balance sheets and making targeted changes to lessor accounting. ASU 2016-02 will be effective beginning in the first quarter of 2019, with early adoption permitted. ASU 2016-02 requires a modified retrospective transition approach for all leases existing at, or entered into after, the date of initial application, with an option to use certain transition relief. Management is currently evaluating the impact of adopting ASU 2016-02 on the Company's consolidated financial statements.

Statement of cash flows

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230)* ("ASU 2016-15"), a consensus of the FASB's Emerging Issues Task Force ("EITF"). ASU 2016-15 is intended to reduce diversity in practice in how certain transactions are classified in the statement of cash flows and requires companies, among other matters, to use reasonable judgment to separate cash flows. Specifically, in the absence of specific guidance, ASU 2016-15 prescribes that an entity should classify each separately identifiable cash source and use on the basis of the nature of the underlying cash flows. ASU 2016-15 is effective for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. Management is currently evaluating the potential impact that this guidance may have on the Company's consolidated financial statements.

In November 2016, the FASB issued ASU No. 2016-18, *Statement of Cash Flows (Topic 230): Restricted Cash* ("ASU 2016-18"), a consensus of the FASB's EITF. ASU 2016-18 requires that the statement of cash flows explain the change during the period in the total of cash, cash equivalents and amounts generally described as restricted cash or restricted cash equivalents. Entities will also be required to reconcile such total to amounts on the balance sheet and disclose the nature of the restrictions. ASU 2016-18 is effective for financial statements issued for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. Management is currently evaluating the potential impact that this guidance may have on the Company's consolidated financial statements.

Stock-based compensation

In May 2017, the FASB issued ASU No. 2017-09, *Compensation—Stock Compensation (Topic 718): Scope of Modification Accounting* ("ASU 2017-09"), which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. Per ASU 2017-09, modification accounting is required only if the fair value, the vesting conditions, or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions, whereas under previous guidance, judgments about whether certain changes to an award are substantive may impact whether or not modification accounting is applied in certain situations. ASU 2017-19 is effective prospectively for annual periods beginning on or after December 15, 2017, with early adoption permitted. Management is currently evaluating the potential impact that this guidance may have on the Company's consolidated financial statements.

2. Net Loss per Share Attributable to Common Stockholders

The outstanding securities presented below were excluded from the calculation of net loss per share attributable to common stockholders, because such securities would have been anti-dilutive due to the Company's net loss per share attributable to common stockholders during the periods ending on the dates presented.

	September 30, 2017	September 30, 2016
Options to purchase common stock	6,134,301	4,888,522
Warrants to purchase common stock	87,901	87,901
Unvested restricted common stock	10,000	25,859
Redeemable convertible preferred stock	740,126	—

3. Held-to-maturity Investments

The following tables provide information relating to the Company's held-to-maturity investments:

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
As of September 30, 2017:				
Held-to-maturity investments				
U.S. treasury securities maturing in one year or less	$ 44,959	$ 1	$ (9)	$44,951

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
As of December 31, 2016:				
Held-to-maturity investments				
U.S. treasury securities maturing in one year or less	$ 25,009	$ —	$ (5)	$25,004

4. Redeemable Convertible Preferred Stock

On April 11, 2017, pursuant to a redeemable convertible preferred stock purchase agreement ("SPA") with seven institutional investors ("Investors"), led by funds advised by Bain Capital Life Sciences L.P. ("Lead Investor"), the Company issued and sold in a private placement 700,000 shares of its newly designated Redeemable Convertible Preferred Stock, par value $0.0001 per share ("Redeemable Convertible Preferred"), at a purchase price of $100.00 per share, for total gross proceeds of $70.0 million ("Private Placement"), less issuance costs of approximately $0.8 million. The shares of Redeemable Convertible Preferred and the shares of common stock issuable upon conversion of the Redeemable Convertible Preferred were offered and sold by the Company pursuant to an exemption from the registration requirements of the Securities Act provided by Section 4(a)(2) thereunder.

In addition to the Lead Investor, other participants in the Private Placement included Cormorant Asset Management, Domain Associates, EcoR1 Capital, RA Capital and Skyline Ventures, among others. Domain Associates, RA Capital and Skyline Ventures are entities that are affiliated or were formerly affiliated with certain members of the Company's board of directors.

The Redeemable Convertible Preferred has the rights and preferences set forth in a Certificate of Designation, which was filed with the Secretary of State of the State of Delaware. Those rights and preferences are summarized below.

Conversion

The Company has the right to require the Investors to convert the Redeemable Convertible Preferred into common stock at any time following the earlier of the second anniversary of the closing of the Private Placement or the occurrence of certain agreed-upon milestone events (the "Milestone Events"), defined as the occurrence of both of the following: (a) (1) the time that the Company first administers a dose of a lead pharmaceutical product candidate to a human being pursuant to an Investigational New Drug ("IND") application filed with the United States Food and Drug Administration ("FDA") or (2) after the Company has first administered a dose of a product candidate to a human being pursuant to a Clinical Trial Application with the Medicine and Healthcare Products Regulatory Agency in the European Union and an IND relating to such product candidate has become effective; and (b) the Company enters into a partnership or license agreement with a major company in the pharmaceutical or biotechnology industry relating to a non-lead product candidate, pursuant to which such company provides the Company with an upfront cash payment of at least a minimum agreed-upon amount and agrees to customary future milestone and royalty payments. In addition to the Milestone Events, the trading price of the Company's common stock must exceed 200% of $3.19 (the "Conversion Price") for 45 out of 60 consecutive trading days in order for the Company to require conversion.

The Company's ability to require conversion shall be subject to (i) a 19.99% blocker provision to comply with NASDAQ Listing Rules ("19.99% Conversion Blocker"), (ii) for certain Investors, a 9.99% blocker provision ("9.99% Conversion Blocker") that will prohibit beneficial ownership of more than 9.99% of the outstanding shares of the Company's common stock or voting power at any time, or (iii) applicable regulatory restrictions. The 19.99% Conversion Blocker and the 9.99% Conversion Blocker are hereinafter referred to as the "Conversion Blockers." The Conversion Price is subject to proportionate adjustment for any stock split, stock dividend, combination or other similar recapitalization event.

Following the date of a required conversion at the Company's option, any shares of Redeemable Convertible Preferred that are not converted as a result of the Conversion Blockers or applicable regulatory restrictions shall continue to be entitled to all of the rights of the holders of Redeemable Convertible Preferred except that they will no longer be entitled to further accrual of dividends, priority distribution of assets upon consummation of a change of control or a liquidation event and certain special voting provisions (see below).

At any time and from time to time at their election, the holders of Redeemable Convertible Preferred will have the option to convert the Redeemable Convertible Preferred into shares of the Company's common stock by dividing (i) the sum of the Accrued Value plus an amount equal to all accrued or declared and unpaid dividends on the Redeemable Convertible Preferred that have not previously been added to the Accrued Value by (ii) the Conversion Price in effect at the time of such conversion. The conversion of shares of Redeemable Convertible Preferred into shares of common stock is subject to the Conversion Blockers. "Accrued Value" means, with respect to each share of Redeemable Convertible Preferred, the sum of (i) $100.00 plus (ii) on each quarterly dividend date, an additional amount equal to the dollar value of any dividends on a share of Redeemable Convertible Preferred which have accrued on any dividend payment date and have not previously been added to such Accrued Value.

Redemption

On or at any time following the seventh anniversary of the closing of the Private Placement, (i) the Company shall have the right to redeem the Redeemable Convertible Preferred for a cash consideration equal to the sum of the Accrued Value, as of the date of redemption, plus an amount equal to all accrued or declared and unpaid dividends on the Redeemable Convertible Preferred that have not previously been added to the Accrued Value, and (ii) the holders of a majority of the Redeemable Convertible Preferred shall also have the right to cause the Company to redeem the Redeemable Convertible Preferred at the same price.

Upon consummation of a specified change of control transaction, each holder of Redeemable Convertible Preferred will be entitled to receive in preference to the holders of common stock and any junior preferred stock, an amount equal to the greater of (i) 101% of the sum of the Accrued Value plus an amount equal to all accrued or declared and unpaid dividends on the Redeemable Convertible Preferred that have not previously been added to the Accrued Value, or (ii) the amount that such shares would have been entitled to receive if they had converted into common stock immediately prior to such event.

Liquidation preferences

In the event of the Company's liquidation, dissolution or winding up, the holder of each share of Redeemable Convertible Preferred will be entitled to receive, in preference to the holders of the common stock and any junior preferred stock, an amount per share equal to the greater of (i) the sum of the Accrued Value plus an amount equal to all accrued or declared and unpaid dividends on the Redeemable Convertible Preferred that have not previously been added to the Accrued Value, or (ii) the amount that such shares would have been entitled to receive if they had converted into common stock immediately prior to such liquidation, dissolution or winding up.

Voting and other rights

Except as set forth above or as otherwise required by law, holders of shares of Redeemable Convertible Preferred are entitled to vote together with shares of common stock (based on one vote per share of common stock into which the shares of Redeemable Convertible Preferred are convertible on the applicable record date) on any matter on which the holders of common stock are entitled to vote.

Additionally, for so long as any shares of Redeemable Convertible Preferred remain outstanding, without the approval of holders of a majority of the Redeemable Convertible Preferred, the Company may not, among other things, (i) amend, modify or fail to give effect to any right of holders of the Redeemable Convertible Preferred, (ii) change the authorized number of Redeemable Convertible Preferred or issue additional Redeemable Convertible Preferred or create a new class or series of equity securities or securities convertible into equity securities with equal or superior rights, preferences or privileges to those of the Redeemable Convertible Preferred in terms of liquidation preference, dividend rights or certain governance rights, (iii) issue shares of common stock or securities convertible into common stock while the Company has insufficient shares to effect the conversion of the Redeemable Convertible Preferred into common stock, (iv) declare or pay dividends or redeem or repurchase any capital stock (other than certain repurchases from employees, directors, advisors or consultants upon termination of service) or (v) incur certain indebtedness in excess of $10 million.

On March 28, 2017, in accordance with the terms of the SPA, the Company increased the size of its board of directors from eight to nine directors and approved the appointment of Adam M. Koppel, M.D., Ph.D., a managing director of the Lead Investor, as a director of the Company, effective as of the closing of the Private Placement on April 11, 2017. To the extent that such director is not re-elected at any time and, so long as the Lead Investor owns at least 25% of the Redeemable Convertible Preferred (or underlying common stock) owned by it at the closing of the Private Placement, the Lead Investor shall have the right to designate a board observer.

The Company also entered into an amended and restated registration rights agreement, by and among the Company and the Investors ("Registration Rights Agreement"). Pursuant to the Registration Rights Agreement, the Investors will be entitled to certain demand, shelf and "piggyback" registration rights with respect to the shares of common stock issuable upon conversion of the Redeemable Convertible Preferred, subject to the limitations set forth in the Registration Rights Agreement.

Dividends

Each holder of Redeemable Convertible Preferred is entitled to receive cumulative dividends on the Accrued Value of each share of Redeemable Convertible Preferred at an initial rate of 12% per annum, compounded quarterly and subject to two rate reductions, of 4% each in connection with the occurrence of one of the Milestone Events (see also Note 8). Dividends on the Redeemable Convertible Preferred are payable in kind and will accrue on the Accrued Value of each share of Redeemable Convertible Preferred until the earlier of conversion, redemption, consummation of a change of control, a liquidation event, or upon failure to mandatorily convert due to the Conversion Blockers or applicable regulatory restrictions.

For accounting purposes, in accordance with the FASB's Accounting Standard Codification ("ASC") Topic 480-10-S99, *Distinguishing Liabilities from Equity — SEC Materials* ("ASC 480-10-S99"), the Company records the additional shares issued as dividends at fair value at each declaration date. The fair value of the dividends is determined using a binary lattice model that captures the intrinsic value of the underlying common stock on the declaration date and the option value of the shares and future dividends. During the three and nine months ended September 30, 2017, the Company issued an aggregate of 21,722 and 40,126 additional shares, respectively, of Redeemable Convertible Preferred as payment in kind of cumulative dividends. These dividends were charged against additional paid-in capital and increased the carrying value of the Redeemable Convertible Preferred on each dividend date.

The lattice model used to determine fair value of dividends on each dividend date through September 30, 2017 included the following inputs:

	As of September 30, 2017	As of June 30, 2017
Price per common share	$ 5.75	$ 3.17
Expected term (in years)	6.50	6.75
Expected volatility	73.0%	70.0%
Risk-adjusted discount rate	19.1%	18.0%

In addition to the inputs presented above, use of the lattice model applies other assumptions, including probability simulations of various outcomes largely associated with the conversion-related milestone events referred to above and with the progression of the Company's per common share price. Use of the lattice model resulted in a fair value estimate of the dividends declared during the three and nine months ended September 30, 2017 of approximately $4.1 million and $6.0 million, respectively.

Classification and measurement

At the date of issuance, the Redeemable Convertible Preferred was classified as temporary equity in the mezzanine section of the Company's consolidated balance sheet, since the underlying preferred shares are subject to redemption upon the occurrence of uncertain events not solely within the Company's control, pursuant to ASC 480-10-S99. As of September 30, 2017, the Redeemable Convertible Preferred was not currently redeemable, and management concluded that it is not probable that the Redeemable Convertible Preferred will become redeemable, primarily due to the existence of the conversion right held by the Company, as discussed above.

In accordance with ASC Topic 470-20, *Debt with Conversion and Other Options* , the Company recorded a beneficial conversion feature ("BCF") related to the issuance of the Redeemable Convertible Preferred. The BCF was recognized separately at issuance by allocating a portion of the proceeds equal to the intrinsic value of that feature to additional paid-in capital. The BCF was calculated at the commitment date, which management has determined to be the date of issuance. Intrinsic value is calculated as the difference between the effective conversion price and the fair value of the Company's common stock, multiplied by the number of shares into which the issued shares of Redeemable Convertible Preferred are convertible. During the nine months ended September 30, 2017, the Company recorded a deemed dividend charge of $6.1 million, to reflect full and immediate accretion of the discount resulting from the at-issuance BCF embedded within the Redeemable Convertible Preferred as a result of the shares being immediately convertible into shares of the Company's common stock at the option of the Investors.

Accretion of the discount resulting from the BCF and cumulative dividends, including accretion of share issuance costs, were non-cash transactions and have been reflected below net loss to arrive at net loss attributable to common stockholders.

The following table reflects the changes in Redeemable Convertible Preferred.

Balance at January 1, 2017	$ —
Issuance of Redeemable Convertible Preferred	70,000
Share issuance costs	(750)
Net proceeds	69,250
Discount resulting from the BCF at issuance	(6,144)
Accretion of the discount resulting from the BCF (deemed dividend)	6,144
Dividends accrued at the stated rate	4,014
Accretion of share issuance costs (additional dividends)	750
Liquidation preference	74,014
Fair value in excess of dividends accrued at the stated rate	1,969
Balance at September 30, 2017	$75,983

No shares of Redeemable Convertible Preferred have been converted since the original issuance thereof through September 30, 2017. As of September 30, 2017, 22,632,433 shares of common stock were issuable upon full conversion of all outstanding shares of the Redeemable Convertible Preferred, after application of the Conversion Blockers, resulting in 43,480,187 total shares of common stock outstanding and approximately 72% ownership of the Company by the Investors on an as-converted, pro-forma basis.

5. Stock Option Plan and Stock-Based Compensation

During the three and nine month periods ended September 30, 2017, the Company granted stock options to purchase 304,500 and 1,635,497 shares of common stock to employees with aggregate grant date fair values of $0.7 million and $3.5 million, respectively, compared to stock options to purchase 30,000 and 1,475,275 shares of common stock granted to employees with aggregate grant date fair values of $0.1 million and $6.9 million, respectively, for the comparable three and nine month periods in 2016.

The assumptions used to estimate the grant date fair value using the Black-Scholes option pricing model were as follows:

	Three Months Ended September 30, 2017	Nine Months Ended September 30, 2017
Common stock price	$ 3.24 – $3.99	$ 2.49 – $3.99
Expected option term (in years)	5.50 – 6.25	5.50 – 6.25
Expected volatility	79.6% – 90.8%	79.4% – 90.8%
Risk-free interest rate	1.87% – 2.04%	1.86% – 2.07%
Expected dividend yield	0.00%	0.00%

	Three Months Ended September 30, 2016	Nine Months Ended September 30, 2016
Common stock price	$ 3.21	$ 3.21 – $9.09
Expected option term (in years)	6.25	5.50 – 6.25
Expected volatility	76.1%	70.9% – 76.1%
Risk-free interest rate	1.17%	1.17% – 1.71%
Expected dividend yield	0.00%	0.00%

The Company has classified stock-based compensation in its condensed consolidated statements of operations as follows:

	Three Months Ended September 30, 2017	Nine Months Ended September 30, 2017	Three Months Ended September 30, 2016	Nine Months Ended September 30, 2016
Research and development expenses	$ 899	$ 2,816	$ 1,163	$ 3,464
General and administrative expenses	1,071	3,187	1,109	3,603
Total	$ 1,970	$ 6,003	$ 2,272	$ 7,067

6. Fair Value Measurements

A summary of the Company's assets that are measured or disclosed at fair value as of September 30, 2017 and December 31, 2016 are presented below:

Description	As of September 30, 2017	Level 1	Level 2	Level 3
Cash equivalents				
Money market fund	$ 26,232	$26,232	$ —	$ —
Held-to-maturity investments				
U.S. treasury securities	44,951	—	44,951	—
Restricted cash equivalents				
Money market fund	1,116	—	1,116	—
Total	$ 72,299	$26,232	$46,067	$ —

Description	As of December 31, 2016	Level 1	Level 2	Level 3
Cash equivalents				
Money market fund	$ 12,853	$12,853	$ —	$ —
Held-to-maturity investments				
U.S. treasury securities	25,004	—	25,004	—
Restricted cash equivalents				
Money market fund	1,116	—	1,116	—
Total	$ 38,973	$12,853	$26,120	$ —

The Company's cash equivalents, which are in money market funds, are classified within Level 1 of the fair value hierarchy because they are valued using quoted prices as of September 30, 2017 and December 31, 2016.

The Company's restricted cash equivalents bore interest at the prevailing market rates for instruments with similar characteristics and, accordingly, the carrying value of these instruments also approximated their fair value. These financial instruments were classified within Level 2 of the fair value hierarchy, because the inputs to the fair value measurement are valued using observable inputs as of September 30, 2017 and December 31, 2016.

The Company's held-to-maturity investments bore interest at the prevailing market rates for instruments with similar characteristics. The financial instruments were classified within Level 2 of the fair value hierarchy, because the inputs to the fair value measurement are valued using observable inputs as of September 30, 2017 and December 31, 2016.

As of September 30, 2017 and December 31, 2016, the carrying amounts of accounts payable and accrued expenses approximated their estimated fair values because of the short-term nature of these financial instruments.

For the three and nine month periods ended September 30, 2017 and 2016 there were no transfers between Level 1 and Level 2.

7. Commitments and Contingencies

Facility lease

Future minimum lease payments on the Company's non-cancelable operating lease for office and laboratory space are as follows:

12-Month Periods Ending September 30,	Operating Lease
2018	$ 1,618
2019	1,666
2020	1,716
2021*	287
Total	$ 5,287

* The end of the lease term is November 30, 2020.

Litigation

On June 10, 2015, Alnylam Pharmaceuticals, Inc. ("Alnylam") filed a complaint against the Company in the Superior Court of Middlesex County, Massachusetts (the "Court"). The complaint alleges misappropriation of confidential, proprietary, and trade secret information, as well as other related claims, in connection with the Company's hiring of a number of former employees of Merck & Co., Inc. ("Merck") and its discussions with Merck regarding the acquisition of its subsidiary, Sirna Therapeutics, Inc., which was subsequently acquired by Alnylam. The complaint seeks among other things, unspecified damages, attorneys' fees, and an order permanently enjoining the Company from disclosing or using any of Alnylam's confidential information or trade secrets. The Court has set a trial date of April 23, 2018.

The Company believes that these allegations lack merit, has filed an answer denying all liability and intends to continue to vigorously defend all claims asserted. At this time, the Company has not recorded a liability in connection with these matters because management believes that any potential loss is neither probable nor reasonably estimable.

From time to time, the Company may be subject to various claims and legal proceedings. If the potential loss from any claim, asserted or unasserted, or legal proceeding is considered probable and the amount is reasonably estimable, the Company will accrue a liability for the estimated loss. There were no litigation liabilities recorded as of September 30, 2017 or December 31, 2016.

8. Subsequent Events

On October 27, 2017, the Company entered into a collaborative research and license agreement with Boehringer Ingelheim International GmbH ("BI") (the "BI Agreement"), pursuant to which the Company and BI will jointly research and develop product candidates that target a specific disease-linked gene in the hepatocytes for the treatment of chronic liver disease using the GalXC platform, Dicerna's proprietary RNAi-based technology. The BI Agreement is for the development of product candidates against one target gene with an option for BI to add the development of product candidates that target a second gene. Also pursuant to the BI Agreement, Dicerna granted BI a worldwide license in connection with the research and development of the product candidates and will transfer to BI intellectual property rights of the product candidates selected by BI for clinical development and commercialization. Dicerna also may provide assistance to BI in order to help BI further develop selected product candidates. Under the terms of the BI Agreement, BI agreed to pay Dicerna a non-refundable upfront payment of $10.0 million. During the term of the research program, BI will reimburse Dicerna the cost of materials and third party expenses that have been included in the preclinical studies up to an agreed-upon limit. The Company is eligible to receive up to $191.0 million in potential development and commercial milestones. Dicerna is also eligible to receive royalty payments on potential global net sales, subject to certain adjustments, tiered from high single digits up to low double-digits. BI's option to add a second target would provide for an option fee payment and success-based development and commercialization milestones and royalty payments to Dicerna.

Entering into the BI Agreement constitutes, per the Certificate of Designation, a Milestone Event for purposes of applying the first of two allowable rate reductions to dividends payable on the Redeemable Convertible Preferred. As such, the dividend rate on the Redeemable Convertible Preferred is subject to reduction from 12% to 8%.

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

The following discussion contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those discussed here. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in this section as well as factors described in Part II, Item 1A—"Risk Factors."

Overview

Founded in 2006 as a Delaware corporation, Dicerna is a biopharmaceutical company focused on the discovery and development of innovative subcutaneously delivered RNAi-based pharmaceuticals using our GalXC ™ RNAi platform for the treatment of diseases involving the liver, including rare diseases, chronic liver diseases, cardiovascular diseases and viral infectious diseases. Within these therapeutic areas, we believe our GalXC RNAi platform will allow us to build a broad pipeline with commercially attractive pharmaceutical properties, including a subcutaneous route of administration, infrequent dosing (e.g., dosing that is monthly or quarterly, and potentially even less frequent), high therapeutic index, and specificity to a single target gene.

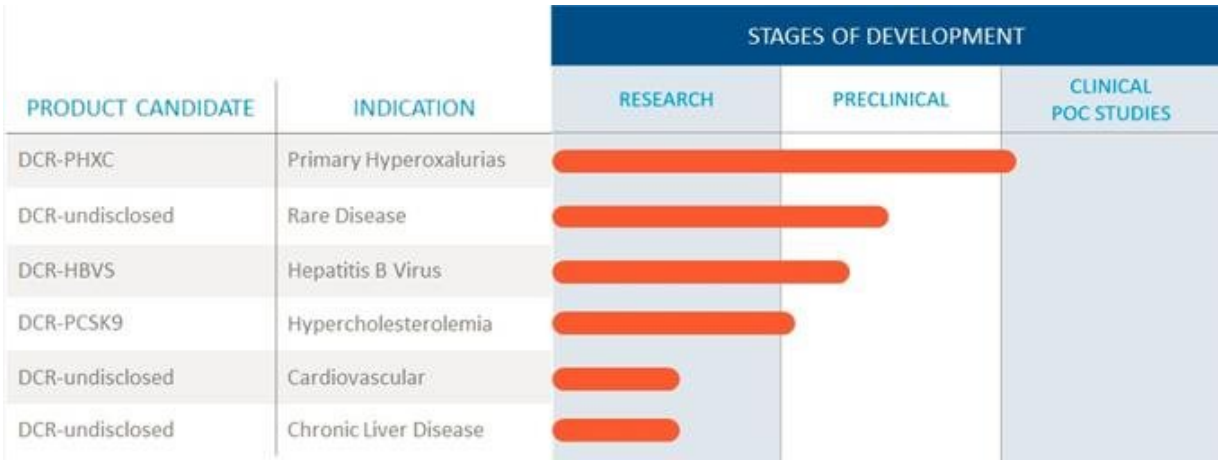
All of our GalXC drug discovery and development efforts are based on the therapeutic modality of RNAi, a highly potent and specific mechanism for silencing the activity of a targeted gene. In this naturally occurring biological process, double-stranded RNA molecules induce the enzymatic destruction of the messenger RNA ("mRNA") of a target gene that contains sequences that are complementary to one strand of the therapeutic double-stranded RNA molecule. The Company's approach is to design proprietary double-stranded RNA molecules that have the potential to engage the enzyme Dicer and initiate an RNAi process to silence a specific target gene. These proprietary molecules are generally referred to as Dicer Substrate short-interfering RNAs ("DsiRNAs"). Our GalXC RNAi platform utilizes a particular Dicer Substrate structure configured for subcutaneous delivery to the liver. Due to the enzymatic nature of RNAi, a single GalXC molecule incorporated into the RNAi machinery can destroy hundreds or thousands of mRNAs from the targeted gene.

The GalXC RNAi platform supports Dicerna's long-term strategy to retain, subject to the evaluation of potential licensing opportunities as they may arise, a full or substantial ownership stake and to invest internally in diseases with focused patient populations, such as certain rare diseases. We see such diseases as representing opportunities that carry a relatively higher probability of success, with genetically and molecularly defined disease markers, high unmet need, a limited number of Centers of Excellence to facilitate reaching these patients, and the potential for more rapid clinical development programs. For more complex diseases with multiple gene dysfunctions and larger patient populations, we plan to pursue collaborations that can provide the enhanced scale, resources and commercial infrastructure required to maximize these prospects.

Development Programs

In choosing which development programs to advance, we apply scientific, clinical, and commercial criteria that we believe allow us to best leverage our GalXC RNAi platform and maximize value. The Company is focusing its efforts on three priority therapeutic programs that currently have a CTA filed or are in IND/CTA enabling studies and on a series of programs in the clinical candidate selection stage that may be elevated into IND/CTA enabling studies in the future, either on our own or in partnership with larger pharmaceutical companies. Our three priority programs are: DCR-PHXC for the treatment of primary hyperoxaluria ("PH"); a program against an undisclosed rare disease; and DCR-HBVS for the treatment of chronic hepatitis B virus ("HBV") infection. Our programs in clinical candidate selection include DCR-PCSK9 for the treatment of hypercholesterolemia, for which a provisional clinical candidate has been selected, and multiple programs targeting undisclosed targets in chronic liver diseases, cardiovascular diseases and additional rare diseases. We filed a CTA for our lead GalXC product candidate, DCR-PHXC, in October 2017 and expect to file additional CTAs and/or IND applications in 2018 and 2019.

The table below sets forth the state of development of our various product candidates as of November 1, 2017.



Our current development programs are as follows:

- **Primary Hyperoxaluria.** We are developing DCR-PHXC for the treatment of all types of PH. PH is a family of rare inborn errors of metabolism in which the liver produces excessive levels of oxalate, which in turn causes damage to the kidneys and to other tissues in the body. In preclinical models of PH, DCR-PHXC reduces oxalate production to near-normal levels, ameliorating the disease condition.

  On October 16, 2017, we announced that we had submitted a CTA for DCR-PHXC to the Medicines and Healthcare products Regulatory Agency ("MHRA") in the United Kingdom. Once the CTA is authorized by the MHRA and Ethics Committee approval has been obtained, we plan to conduct our Phase 1 trial as a randomized, single-blind, placebo-controlled, single-ascending dose study, enrolling up to 25 healthy volunteer subjects and up to 16 patients with PH. The primary objective of the study is to evaluate the safety and tolerability of single doses of DCR-PHXC, with participants being enrolled into as many as five sequential cohorts of increasing doses. Patients with PH will be dosed after safety has been established at the same dose level in normal healthy volunteers. Secondary endpoints include the pharmacokinetics of DCR-PHXC and its pharmacodynamic effects on oxalate biomarkers in plasma and urine. We plan to commence human clinical trials in the first quarter of 2018 and expect to have clinical proof-of-concept data in the second half of 2018. We also plan to submit additional CTAs in other European countries later this year and an IND application in the U.S. during the first quarter of 2018.

  On July 15, 2017, in a series of presentations at the 12 th International Workshop on Primary Hyperoxaluria for Professionals, Patients and Families in Tenerife, Spain ("12 th International Workshop"), we presented new preclinical data suggesting the potential utility of DCR-PHXC for treating all forms of PH. In particular, we presented research from animal models demonstrating how DCR-PHXC inhibits the lactate dehydrogenase A (" *LDHA* ") gene, which we have identified as potentially being an optimal therapeutic target in patients with PH. *LDHA* inhibition was shown in animal models to reduce oxalate to normal or near-normal levels in PH types 1, 2 and ethylene glycol-induced hyperoxaluria (a model for idiopathic PH).

  LDHA reduction has a near-linear correlation with oxalate reduction and offers a minimal metabolic intervention. These benefits of *LDHA* inhibition may translate into consistent therapeutic activity even in the event of a missed dose. There are numerous case reports of *LDHA* deficiency naturally occurring in humans, with no reported adverse effects due to deficiency in the liver.

To facilitate DCR-PHXC development, we have completed our Primary HYperoxaluria Observational Study ("PHYOS"), an international, multicenter, observational study in patients with a genetically confirmed diagnosis of PH, type 1 ("PH1"). PHYOS is collecting data on key biochemical parameters implicated in the pathogenesis of PH1. We hope to use the data to better understand the baseline PH1 disease state, which will help guide long-term drug development plans. At the 12 th International Workshop, we reported interim data from the study's 20 enrolled patients with a median age at screening of 21 years (range 12-61 years). The patients had been diagnosed at a median age of 7 years (range 1-59 years), and 14 patients (74%) had a medical history of renal stones. Over the six-month observation period, the variability (coefficient of variation) between 24-hour urine measurements of oxalate at different time points was 28%. These data will help our clinical team design future clinical studies using 24-hour urinary oxalate excretion as a surrogate marker for clinical benefit. We expect to publish data from PHYOS in 2018.

- **An undisclosed rare disease involving the liver.** We are developing a GalXC-based therapeutic, targeting a liver-expressed gene involved in a serious rare disease. For competitive reasons, we have not yet publicly disclosed the target gene or disease. We have selected this target gene and disease based on criteria that include having a strong therapeutic hypothesis, a readily-identifiable patient population, the availability of a potentially predictive biomarker, high unmet medical need, favorable competitive positioning and what we believe is a rapid projected path to approval. We plan to file an IND application and/or CTA for this program in the second quarter of 2018.
- **Chronic Hepatitis B Virus infection:** Current therapies for HBV rarely lead to a long-term immunological cure as measured by the clearance of HBV surface antigen ("HBsAg") and sustained HBV deoxyribonucleic acid ("DNA") suppression in patient plasma or blood. We have declared a GalXC RNAi platform-based product candidate, DCR-HBVS, and are conducting formal non-clinical development studies. We expect to file an IND application or a CTA approximately at the end of 2018. DCR-HBVS targets HBV messenger RNA. Based on preclinical studies, and only if we receive appropriate regulatory approval to begin human clinical trials, we hope to determine the potential of DCR-HBVS to reduce HBsAg expression and HBV DNA in HBV patients in a commercially attractive subcutaneous dosing paradigm.
- **Hypercholesterolemia (PCSK9 targeted therapy).** We are using our GalXC RNAi platform to develop a therapeutic that targets the PCSK9 gene for the treatment of hypercholesterolemia. The Company has selected a provisional clinical candidate for the program, but is continuing to explore ways to further optimize the program. PCSK9 is a validated target for hypercholesterolemia, and there are FDA-approved therapies targeting PCSK9 that are based on monoclonal antibody technology. Based on preclinical studies, we believe that our GalXC RNAi platform has the potential to produce a PCSK9-targeted therapy with attractive commercial properties, such as small subcutaneous injection volumes and less frequent dosing.
- **Additional pipeline programs.** We have applied our GalXC technology to multiple gene targets across our disease focus areas of chronic liver diseases, cardiovascular diseases and rare diseases. Pursuant to our strategy, we are seeking collaborations with larger pharmaceutical companies to advance our programs in the areas of chronic liver diseases and cardiovascular diseases. Both these disease areas represent large and diverse patient populations, requiring complex clinical development and commercialization paths that we believe can be more effectively be pursued in partnership with larger pharmaceutical companies more experienced in these types of programs. For our additional rare diseases, we are continuing to assess their potential for clinical success and market opportunity while optimizing our GalXC molecules.

In addition to our GalXC development programs, we have entered into the BI Agreement, pursuant to which the Company and BI will jointly research and develop product candidates that target a specific disease-linked gene in the hepatocytes for the treatment of chronic liver disease using our GalXC platform. The BI Agreement is for the development of product candidates against one target gene with an option for BI to add the development of product candidates that target a second gene. Also pursuant to the BI Agreement, we granted BI a worldwide license in connection with the research and development of the product candidates and will transfer to BI intellectual property rights of the product candidates selected by BI for clinical development and commercialization. We also may provide assistance to BI in order to help BI further develop selected product candidates. Under the terms of the BI Agreement, BI agreed to pay is a non-refundable upfront payment of $10.0 million. During the term of the research program, BI will reimburse us the cost of materials and third party expenses that have been included in the preclinical studies up to an agreed-upon limit. We are eligible to receive up to $191.0 million in potential development and commercial milestones. We are also eligible to receive royalty payments on potential global net sales, subject to certain adjustments, tiered from high single digits up to low double-digits. BI's option to add a second target would provide for an option fee payment and success-based development and commercialization milestones and royalty payments to us.

We are party to a collaboration for our early generation of Dicer Substrate RNAi technology, non-GalXC technology, against two targets, the KRAS oncogene and an additional undisclosed gene, with the global pharmaceutical company, KHK, to use for development in oncology and formulated using KHK's proprietary drug delivery system. KHK is responsible for global development of the KRAS program, including all development expenses. For the KRAS product candidate, we retain an option to co-promote in the U.S. for an equal share of the profits from U.S. net sales. We are also developing, with KHK, a therapeutic candidate targeting a second cancer-related gene, which we are not identifying at this time. For each product candidate in our collaboration with KHK, we have the potential to receive clinical, regulatory and commercialization milestone payments of up to $110.0 million and royalties on net sales of each such product candidate. KHK is responsible for all preclinical and clinical development activities, including the selection of patient population and disease indications for clinical trials. According to information received from KHK, both product candidates are in preclinical development.

We also have developed a wholly owned clinical candidate, DCR-BCAT, targeting the ß-catenin oncogene. DCR-BCAT is based on an extended version of our earlier generation Dicer Substrate RNAi technology and is delivered by our LNP tumor delivery system, EnCore ™ . We plan to out-license or spin out the DCR-BCAT opportunity, given our focus on our GalXC platform-based programs.

Redeemable Convertible Preferred Stock

On April 11, 2017, we issued and sold 700,000 shares of our newly designated Redeemable Convertible Preferred to the Investors in a Private Placement for aggregate gross proceeds of $70.0 million, less issuance costs of approximately $0.8 million. In addition to the Lead Investor, other participants in the Private Placement included Cormorant Asset Management, Domain Associates, EcoR1 Capital, RA Capital and Skyline Ventures, among others. Domain Associates, RA Capital and Skyline Ventures are entities that are affiliated or were formerly affiliated with certain members of our board of directors.

We have the right to require the Investors to convert the Redeemable Convertible Preferred into common stock ("Mandatory Conversion") at any time following the earlier of (i) the second anniversary of the closing of the Private Placement or (ii) the occurrence of both of the following: (a) (1) the date that we first administer, after the issue date, a dose of a pharmaceutical product candidate (which such product candidate shall be one of the following candidates, or a variation thereof: DCR-PHXC, DCR-PCSK9 or the undisclosed rare disease program currently in pre-clinical development (each, a "Product Candidate")) to a human being pursuant to an IND application filed by us with the FDA; or (2) after we have first administered, after the issue date, a dose of a Product Candidate to a human being pursuant to a clinical trial authorization with the Medicine and Healthcare Products Regulatory Agency in the EU and an IND application relating to such Product Candidate has become effective; and (b) the date we enter into a partnership or license agreement with a major company in the pharmaceutical or biotechnology industry relating to a non-Product Candidate, pursuant to which such company provides us with an up-front cash payment of a minimum amount agreed upon by us and the Lead Investor and agrees to customary future milestone and royalty payments, provided, that, in each case ((i) and (ii)), the trading price of our common stock exceeds 200% of the Conversion Price, as defined below, for 45 out of 60 consecutive trading days. Our ability to require conversion shall be subject to the Conversion Blockers and applicable regulatory restrictions. "Conversion Price" shall mean an initial price of $3.19 per share, subject to proportionate adjustment for any stock split, stock dividend, combination or other similar recapitalization event.

Following the date of a Mandatory Conversion, any shares of Redeemable Convertible Preferred that are not converted as a result of the Conversion Blockers or applicable regulatory restrictions shall continue to be entitled to all of the rights of the holders of Redeemable Convertible Preferred except that they will no longer be entitled to further accrual of dividends, priority distribution of assets upon consummation of a change of control or a liquidation event and certain special voting provisions.

On or at any time following the seventh anniversary of the closing of the Private Placement, (i) we shall also have the right to redeem the Redeemable Convertible Preferred for a cash consideration equal to the sum of the Accrued Value, as of the date of redemption, plus an amount equal to all accrued or declared and unpaid dividends on the Redeemable Convertible Preferred that have not previously been added to the Accrued Value, and (ii) the holders of a majority of the Redeemable Convertible Preferred shall also have the right to cause us to redeem the Redeemable Convertible Preferred at the same price. "Accrued Value" means, with respect to each share of Redeemable Convertible Preferred, the sum of (i) $100.00 plus (ii) on each quarterly dividend date, an additional amount equal to the dollar value of any dividends on a share of Redeemable Convertible Preferred which have accrued on any dividend payment date and have not previously been added to such Accrued Value.

At any time and from time to time at their election, the holders of Redeemable Convertible Preferred will have the option to convert the Redeemable Convertible Preferred into shares of our common stock by dividing (i) the sum of the Accrued Value plus an amount equal to all accrued or declared and unpaid dividends on the Redeemable Convertible Preferred that have not previously been added to the Accrued Value by (ii) the Conversion Price in effect at the time of such conversion. The conversion of shares of Redeemable Convertible Preferred into shares of common stock is subject to the Conversion Blockers.

In the event of our liquidation, dissolution or winding up, the holder of each share of Redeemable Convertible Preferred will be entitled to receive, in preference to the holders of the common stock and any junior preferred stock, an amount per share equal to the greater of (i) the sum of the Accrued Value plus an amount equal to all accrued or declared and unpaid dividends on the Redeemable Convertible Preferred that have not previously been added to the Accrued Value, or (ii) the amount that such shares would have been entitled to receive if they had converted into common stock immediately prior to such liquidation, dissolution or winding up.

Upon consummation of a specified change of control transaction, each holder of Redeemable Convertible Preferred will be entitled to receive in preference to the holders of common stock and any junior preferred stock, an amount equal to the greater of (i) 101% of the sum of the Accrued Value plus an amount equal to all accrued or declared and unpaid dividends on the Redeemable Convertible Preferred that have not previously been added to the Accrued Value, or (ii) the amount that such shares would have been entitled to receive if they had converted into common stock immediately prior to such event.

In addition, for so long as any shares of Redeemable Convertible Preferred remain outstanding, without the approval of holders of a majority of the Redeemable Convertible Preferred, we may not, among other things, (i) amend, modify or fail to give effect to any right of holders of the Redeemable Convertible Preferred, (ii) change the authorized number of Redeemable Convertible Preferred or issue additional Redeemable Convertible Preferred or create a new class or series of equity securities or securities convertible into equity securities with equal or superior rights, preferences or privileges to those of the Redeemable Convertible Preferred in terms of liquidation preference, dividend rights or certain governance rights, (iii) issue shares of common stock or securities convertible into common stock while we have insufficient shares to effect the conversion of the Redeemable Convertible Preferred into common stock, (iv) declare or pay dividends or redeem or repurchase any capital stock (other than certain repurchases from employees, directors, advisors or consultants upon termination of service) or (v) incur certain indebtedness in excess of $10 million. Except as set forth above or as otherwise required by law, holders of shares of Redeemable Convertible Preferred are entitled to vote together with shares of common stock (based on one vote per share of common stock into which the shares of Redeemable Convertible Preferred are convertible on the applicable record date) on any matter on which the holders of common stock are entitled to vote.

Per the Certificate of Designation, each holder of Redeemable Convertible Preferred is entitled to receive cumulative dividends on the Accrued Value of each share of Redeemable Convertible Preferred at an initial rate of 12% per annum, compounded quarterly and subject to two rate reductions, of 4% each, upon the occurrence of certain agreed-upon Milestone Events. The dividend rate is subject to reduction from 12% to 8% pursuant to our entry pursuant to our entry into the BI Agreement. Dividends on the Redeemable Convertible Preferred are payable in kind and will accrue on the Accrued Value of each share of Redeemable Convertible Preferred until the earlier of conversion, redemption, consummation of a change of control, a liquidation event, or upon failure to mandatorily convert due to the Conversion Blockers or applicable regulatory restrictions.

In accordance with the terms of the SPA, on March 28, 2017, our board of directors voted to increase the size of the board from eight directors to nine directors and approved the appointment of Adam M. Koppel, M.D., Ph.D., a managing director of the Lead Investor, as a director of our Company, effective as of the closing of the Private Placement on April 11, 2017, to fill the resulting vacancy. To the extent such director is not re-elected at any time and, so long as the Lead Investor owns at least 25% of the Redeemable Convertible Preferred (or underlying common stock) owned by it at the closing of the Private Placement, it shall have the right to designate a board observer. On September 30, 2017, the Lead Investor, which appointed one of its managing directors to our board of directors, owned approximately 19% of the Company on an as-converted basis and after application of the Conversion Blockers.

We also entered into a Registration Rights Agreement, by and among us and the Investors. Pursuant to the Registration Rights Agreement, the Investors will be entitled to certain demand, shelf and “piggyback” registration rights with respect to the shares of common stock issuable upon conversion of the Redeemable Convertible Preferred, subject to the limitations set forth in the Registration Rights Agreement.

The shares of Redeemable Convertible Preferred and the shares of common stock issuable upon conversion of the Redeemable Convertible Preferred were offered and sold by us pursuant to an exemption from the registration requirements of the Securities Act provided by Section 4(a)(2) thereunder.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with GAAP. The preparation of our consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the revenue and expenses incurred during the reported periods. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued expenses and stock-based compensation and in relation to the accounting for the Redeemable Convertible Preferred, including cumulative dividends thereon. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ from these estimates under different assumptions or conditions.

The critical accounting policies that we believe impact significant judgments and estimates used in the preparation of our financial statements presented in this report are described in our Management's Discussion and Analysis of Financial Condition and Results of Operations in our Annual Report on Form 10-K filed with the SEC on March 30, 2017, as amended. There have been no changes to our critical accounting policies during the three or nine month periods ended September 30, 2017 from those discussed in "Management's Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Policies and Significant Judgments and Estimates" in our Annual Report on Form 10-K filed with the SEC on March 30, 2017, as amended, except as related to management's judgment associated with the accounting for, including the valuation of dividends on, the Redeemable Convertible Preferred and as discussed below.

Recent Accounting Pronouncements

A summary of recent accounting pronouncements that have been adopted or are expected to be adopted by the Company is included in Note 1 to our condensed consolidated financial statements (see Part I, Item 1—"Financial Statements" of this Quarterly Report on Form 10-Q). Additional information regarding relevant accounting pronouncements is provided below.

Adopted in 2017

Stock-based compensation

In March 2016, the accounting guidance related to various aspects of share-based payment transactions was amended, including income tax consequences, classification of awards as either equity or liabilities and classification on the statement of cash flows. Under the new guidance, excess tax benefits and deficiencies are to be recognized as income tax expense or benefit in the income statement as discrete items in the reporting period in which they occur instead of an increase or decrease to stockholders' equity. With regard to forfeitures, an entity may make an accounting policy election either to estimate the number of awards that are expected to vest or account for forfeitures when they occur. We adopted this new guidance on January 1, 2017, and as a result, we will track stock option deductions in our net operating loss deferred tax asset on a modified retrospective basis. In addition, our policy has been to estimate forfeitures as of the grant date. We will continue to maintain our policy to estimate forfeiture as of the grant date in the future. Since we historically have maintained a full valuation allowance on our net deferred tax asset, there is no net impact to our accumulated deficit or on our net loss per share attributable to common stockholders from the adoption of this new guidance. As such, adoption of this guidance did not have any impact on our consolidated financial statements.

Not yet adopted

Revenue recognition

In May 2014, the accounting guidance related to revenue recognition was amended to replace current guidance with a single, comprehensive standard for accounting for revenue from contracts with customers. The new guidance will become effective for us on January 1, 2018.

The new revenue standard applies to all contracts with customers, and only contracts with customers are in the scope of the new revenue standard. Once a contractual arrangement is scoped into the new guidance, revenue is recognized based on a model that includes identifying performance obligations and determining and allocating the transaction price to the performance obligations identified in the contract. Revenue is recognized as those performance obligations are satisfied. Entities have the option of using either a full retrospective or a modified retrospective approach to adopt this new guidance.

Our evaluation of the impact that the adoption of this guidance will have on our consolidated financial statements will continue throughout 2017, and while we have not yet determined which adoption method will be utilized or the effect that adoption of this new guidance may have on our consolidated financial statements, we have determined that we will apply the new standard only to contracts that are not completed as of January 1, 2018, as allowed by the standard's transitional guidance. We will evaluate the impact that the new guidance may have on current arrangements with customers, including our collaboration with KHK. As for grant income that currently is recognized as revenue in our consolidated financial statements, we have determined that this item does not meet the definition of revenue under Topic 606 and that, while there will be no cumulative effect on initial adoption of Topic 606 related to our grants, grant income will no longer be presented as revenue in our consolidated statement of operations. Instead, we expect to classify grant-related income as a direct reduction to the research and development expenses to which the grants relate.

Income taxes

New guidance issued in October 2016 related to income taxes is aimed at reducing complexity in accounting standards by eliminating the current exception that the tax effects of intra-entity asset transfers (such as intercompany sales or transfers of intellectual property) be deferred until the transferred asset is sold to a third party or otherwise recovered through use. Instead, the new guidance will require that a reporting entity recognize any tax expense from the sale of the asset in the seller's tax jurisdiction when the transfer occurs, even though the pre-tax effects of that transaction are eliminated in consolidation. Any deferred tax asset that arises in the buyer's jurisdiction would also be recognized at the time of the transfer. This new guidance will be effective for us beginning on January 1, 2018, and we are currently evaluating the potential impact that this guidance may have on our consolidated financial statements. We have not recorded any deferred tax assets or liabilities on our consolidated balance sheet.

Leases

In February 2016, accounting guidance related to leases was issued that will require an entity to recognize leased assets and the rights and obligations created by those leased assets on the balance sheet and to disclose key information about an entity's leasing arrangements. This guidance will become effective for us on January 1, 2019, with early adoption permitted. We expect that the adoption of this guidance will impact our consolidated financial statements and notes thereto, resulting, among other factors, from the recognition of a right of use asset and related liability related to our 2014 non-cancelable operating lease arrangement for our office and laboratory space in Cambridge, Massachusetts. As of September 30, 2017, and as presented below, our total future minimum lease obligation associated with this lease was $5.3 million, and a substantial portion of this commitment will remain outstanding at the time that we adopt the new guidance. Our evaluation of this guidance and its full impact on our consolidated financial statements will continue throughout 2017.

Statement of cash flows

In August 2016, the accounting guidance related to the statement of cash flows was amended with the intent of reducing diversity in practice as to the classification of certain transactions in the statement of cash flows. This guidance will become effective for us on January 1, 2018, with early adoption permitted. Additionally, in November 2016, new accounting guidance was issued related to the statement of cash flows implications related to restricted cash and cash equivalents. This new guidance is effective for us beginning on January 1, 2018, and we will continue to evaluate the impact that the guidance may have on our consolidated financial statements, particularly as pertaining to our restricted cash equivalents.

Stock-based compensation

In May 2017, the accounting guidance related to stock-based compensation was amended to clarify when to account for a change to the terms or conditions of a share-based payment award as a modification. Per the new guidance, modification accounting is required only if the fair value, the vesting conditions, or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions, whereas under previous guidance, judgments about whether certain changes to an award are substantive may impact whether or not modification accounting is applied in certain situations. This new guidance is effective prospectively for annual periods beginning on or after December 15, 2017, with early adoption permitted. We are currently evaluating the potential impact that this guidance may have on our consolidated financial statements.

Financial Operations Overview

Comparison of the Three and Nine Month Periods Ended September 30, 2017 and 2016

The following table summarizes the results of our operations for the periods indicated (in thousands, except percentages).

	Three Months Ended September 30, 2017	Three Months Ended September 30, 2016	Increase/ (Decrease)		Nine Months Ended September 30, 2017	Nine Months Ended September 30, 2016	Increase/ (Decrease)	
Revenue	$ 474	$ 162	$ 312	192.6%	$ 859	$ 162	$ 697	430.2%
Expenses:								
Research and development	9,001	10,061	(1,060)	(10.5%)	27,197	32,357	(5,160)	(15.9%)
General and administrative	6,685	4,338	2,347	54.1%	18,481	13,478	5,003	37.1%
Total operating expenses	15,686	14,399	1,287	8.9%	45,678	45,835	(157)	(0.3%)
Loss from operations	(15,212)	(14,237)	975	6.8%	(44,819)	(45,673)	(854)	(1.9%)
Interest income	179	61	118	193.4%	360	182	178	97.8%
Net loss	(15,033)	(14,176)	857	6.0%	(44,459)	(45,491)	(1,032)	(2.3%)
Dividends on redeemable convertible preferred stock	(4,111)	—	4,111	—	(6,733)	—	6,733	—
Deemed dividend related to beneficial conversion feature of redeemable convertible preferred stock	—	—	—	—	(6,144)	—	6,144	—
Net loss attributable to common stockholders	$ (19,144)	$ (14,176)	$ 4,968	35.0%	$ (57,336)	$ (45,491)	$11,845	26.0%

Revenue

Revenue recognized during the three and nine month periods ended September 30, 2017 relates to NIH grant awards for cancer treatment research (the "Project"), totaling $2.0 million and covering the period from September 1, 2016 to February 28, 2018. $1.0 million of the Project grant was awarded in August 2016, and on September 1, 2017, we were awarded an additional grant in the amount of $1.0 million for the Project. To date, we have recognized approximately $1.2 million of revenue in connection with the Project grant awards, and we expect to recognize the remaining $0.8 million over the next two quarters.

Grant revenue represents reimbursable subcontractor and internal costs incurred that are specifically covered by the grant, and where applicable, funding for qualifying facilities and administrative expenses. As noted above, upon adoption of Topic 606, we no longer will present grant income as revenue in our consolidated statement of operations; instead, we will present grant income as a direct reduction to the research and development expenses to which the grants relate.

We do not expect to generate any product revenue for the foreseeable future. However, we expect to begin recognizing revenue, beginning in the fourth quarter of 2017, in connection with the BI Agreement.

Research and development expenses

The following table summarizes our research and development expenses incurred during the periods indicated (in thousands):

	Three Months Ended September 30,		
	2017	2016	Increase/ (Decrease)
Direct research and development expenses	$ 3,809	$ 3,105	$ 704
Employee-related expenses	2,567	2,912	(345)
Platform-related expenses	1,883	3,254	(1,371)
Facilities, depreciation and other expenses	742	790	(48)
Total	$ 9,001	$ 10,061	$ (1,060)

	Nine Months Ended September 30,		
	2017	2016	Increase/ (Decrease)
Direct research and development expenses	$11,289	$10,330	$ 959
Employee-related expenses	8,133	10,075	(1,942)
Platform-related expenses	5,424	9,257	(3,833)
Facilities, depreciation and other expenses	2,351	2,695	(344)
Total	$27,197	$32,357	$ (5,160)

The increase in direct research and development expenses in both the three and nine month periods ended September 30, 2017 is attributable to an overall increase in manufacturing activities and in toxicology study costs related to our product candidates under our GalXC platform, partially offset by a reduction in clinical and manufacturing activities related to our now discontinued DCR-PH1 and DCR-MYC programs, which were not based on our GalXC platform. Employee-related expenses decreased in both the three and nine month periods ended September 30, 2017 as compared to the corresponding periods in 2016 due to an overall decrease in headcount from the prior year periods, along with a decrease in non-cash stock-based compensation costs. Platform-related expenses decreased substantially in both the three and nine month periods ended September 30, 2017 as compared to the corresponding periods in 2016 due to the timing of activities related to discovery and early development programs, including supply and external study costs.

We expect our overall research and development expenses to increase during the fourth quarter of 2017, as compared to the third quarter of 2017, primarily as we ramp up our clinical initiatives associated with DCR-PHXC.

General and administrative expenses

General and administrative expenses were $6.7 million and $18.5 million for the three and nine months ended September 30, 2017, as compared to $4.3 million and $13.5 million for the three and nine months ended September 30, 2016, respectively. The increases are predominantly related to higher costs associated with the litigation with Alnylam as well as to higher salaries, benefits and other employee-related expenses.

Interest income

Interest income is comprised primarily of interest earned from our money market accounts and held-to-maturity investments. Interest income was $0.2 million and $0.4 million for the three and nine months ended September 30, 2017, respectively, as compared to $0.1 million and $0.2 million for the three and nine months ended September 30, 2016, respectively. The increases were primarily due to higher invested amounts in the 2017 periods as a result of the net proceeds from the Private Placement, which closed in the second quarter of 2017.

Dividends

Dividends of $4.1 million and $6.7 million recorded during the three and nine months ended September 30, 2017, respectively, represent the non-cash fair value of additional shares of Redeemable Convertible Preferred issued to the Investors as dividends paid in kind, as well as, for the nine-month period ended September 30, 2017, full accretion of share issuance costs. The fair value of the issued shares was determined using a binary lattice model that captures the intrinsic value of the underlying common stock on the declaration date and the option value of the shares and future dividends. Inputs to the lattice model include an adjusted risk rate, our common stock volatility, the underlying common stock price on the dividend date and management's judgment associated with probability simulations of various outcomes. Dividends are valued at each dividend declaration date, based on various inputs and assumptions at that time, and, as such, quarterly dividend amounts may vary significantly from quarter to quarter. No common stock dividends were recorded during the three or nine month periods ended September 30, 2017.

The deemed dividend of $6.1 million (non-cash) for the nine months ended September 30, 2017 represents the value of the BCF, which was accreted in full at issuance due to the fact that the underlying shares of Redeemable Convertible Preferred are immediately convertible. Management is required to evaluate whether a BCF exists at each Redeemable Convertible Preferred issuance date. Consequently, the intrinsic value of any future shares of Redeemable Convertible Preferred issued as dividends will be recorded as additional deemed dividends in future quarters.

Net loss attributable to common stockholders

Net loss attributable to common stockholders was $19.1 million and $57.3 million for the three and nine months ended September 30, 2017, as compared to $14.2 million and $45.5 million for the same periods in 2016, respectively. The overall increases in net loss attributable to common stockholders are due to the aforementioned changes in research and development and general and administrative expenses, as well as to the recording of dividends in 2017 on the Redeemable Convertible Preferred.

Liquidity and Capital Resources

As of September 30, 2017, we had cash and cash equivalents and held-to-maturity investments of $75.9 million and $1.1 million in cash equivalents held in restriction.

Aggregate gross proceeds received on April 11, 2017 in connection with the closing of the Private Placement totaled $70.0 million, less related transaction costs of approximately $0.8 million.

On October 31, 2016, a universal shelf registration statement on Form S-3 permitting the sale of up to $150.0 million of our common stock and other securities was declared effective by the SEC. Additionally, we are currently permitted to sell, from time to time through April 2, 2018: (i) up to 10,000,000 shares of our common stock; (ii) up to a maximum aggregate offering price of $50,000,000 of preferred stock, debt securities, warrants or units; and (ii) up to 2.5 million shares of our common stock at market prices prevailing at the time of the sale pursuant to a universal shelf registration statement on Form S-3 declared effective by the SEC on April 2, 2015. As of November 2, 2017, we have sold 2,750,000 shares of our common stock pursuant to these universal shelf registration statements.

Cash flows

The following table shows a summary of our cash flows for the periods indicated (in thousands):

	Nine Months Ended September 30,	
	2017	2016
Net cash used in operating activities	$(39,373)	$(37,157)
Net cash (used in) provided by investing activities	(19,986)	13,109
Net cash provided by financing activities	69,454	534
Increase (decrease) in cash and cash equivalents	$ 10,095	$(23,514)

Operating activities

Net cash used in operating activities was $39.4 million for the nine months ended September 30, 2017, as compared to $37.2 million for the nine months ended September 30, 2016. The increase of $2.2 million was primarily due to higher general and administrative expenses and negative working capital fluctuations, partially offset by lower overall research and development expenses.

We expect our cash used in operating activities during the last quarter of 2017 to be significantly lower than the average quarterly cash used in our operating activities for the nine month period ended September 30, 2017, predominantly due to the aforementioned upfront proceeds expected to be received from BI, and despite the ongoing ramp-up of clinical initiatives associated with our lead product candidates.

Investing activities

Net cash used in investing activities was $20.0 million for the nine months ended September 30, 2017, as compared to net cash provided by investing activities of $13.1 million for the nine months ended September 30, 2016. This change was due primarily to $64.9 million of purchases of held-to-maturity investments, partially offset by $45.0 million in maturities of held-to-maturity investments during the nine months ended September 30, 2017, as compared to $20.0 million in purchases of held-to-maturity investments, partially offset by $33.5 million of maturities of held-to-maturity investments, during the nine months ended September 30, 2016.

Financing activities

Net cash provided by financing activities was $69.5 million for the nine months ended September 30, 2017, as compared to $0.5 million for the nine months ended September 30, 2016. The increase of $68.9 million was principally due to the receipt of $69.3 million in gross proceeds from the Private Placement, partially offset by lower proceeds received in connection with stock option exercises and with issuances under the employee stock purchase plan.

Funding requirements

We expect that our primary uses of capital will continue to be third-party clinical research and development services and manufacturing costs, compensation and related expenses, laboratory and related supplies, legal and other regulatory expenses, including the costs to defend the Alnylam claim of misappropriation of confidential information and trade secrets, and general overhead costs. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates and the extent to which we may enter into additional collaborations with third parties to participate in their development and commercialization, we are unable to estimate the amounts of capital outlays and operating expenditures associated with our anticipated development activities. However, based on our current operating plan, we believe that available cash, cash equivalents and held-to-maturity investments and the receipt of upfront proceeds in connection with the BI Agreement will be sufficient to fund our planned level of operations for at least the 12-month period following November 2, 2017. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect.

Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially as a result of a number of factors. Our future capital requirements are difficult to forecast and will depend on many factors, including:

- the receipt of milestone payments under our collaboration agreements with BI and KHK;
- the terms and timing of any other collaboration, licensing and other arrangements that we may establish;
- the initiation, progress, timing and completion of preclinical studies and clinical trials for our potential product candidates;
- the number and characteristics of product candidates that we pursue;
- the outcome, timing and cost of regulatory approvals;
- delays that may be caused by changing regulatory requirements;
- the cost and timing of hiring new employees to support our continued growth;
- the costs involved in filing and prosecuting patent applications and enforcing and defending patent claims;
- the costs of filing and prosecuting intellectual property rights and enforcing and defending any intellectual property-related claims;
- the costs of responding to and defending ourselves against complaints and potential litigation, including the Alnylam complaint of misappropriation of confidential information and trade secrets (see Part II, Item 1—"Legal Proceedings" in this Quarterly Report on Form 10-Q);
- the costs and timing of procuring clinical and commercial supplies for our product candidates;
- the extent to which we acquire or in-license other product candidates and technologies; and
- the extent to which we acquire or invest in other businesses, product candidates or technologies.

Until such time, if ever, we generate product revenue, we expect to finance our cash needs through a combination of public or private equity offerings, debt financings and research collaboration and license agreements. We may be unable to raise capital or enter into such other arrangements when needed or on favorable terms, or at all. Our failure to raise capital or enter into such other arrangements in a reasonable timeframe would have a negative impact on our financial condition, and we may have to delay, reduce or terminate our research and development programs, preclinical or clinical trials, limit strategic opportunities or undergo reductions in our workforce or other corporate restructuring activities.

Please see the risk factors set forth in Part II, Item 1A—"Risk Factors" in this Quarterly Report on Form 10-Q for additional risks associated with our substantial capital requirements.

Contractual Obligations and Commitments

The following is a summary of our significant contractual obligations as of September 30, 2017 (in thousands):

	Payments Due By Period				
	Total	Less Than 1 Year	More Than 1 Year and Less Than 3 Years	More Than 3 Years and Less Than 5 Years	More Than 5 Years
Operating lease obligation*	$5,287	$ 1,618	$ 3,382	$ 287	$ —

* Represents future minimum lease payments under our existing non-cancelable operating lease for our office and laboratory space in Cambridge, Massachusetts. The end of the lease term is November 30, 2020.

We also have obligations to make future payments to City of Hope, an independent academic research and medical center ("COH"), Plant Bioscience Limited ("PBL") and the Carnegie Institution of Washington ("Carnegie") that become due and payable on the achievement of certain development, regulatory and commercial milestones. We have not included these commitments on our condensed consolidated balance sheet or in the table above, since the achievement and timing of these milestones are not probable or estimable as of September 30, 2017.

See also Part II, Item 1—"Legal Proceedings" in this Quarterly Report on Form 10-Q for additional information related to litigation. We have not recorded any accrual for contingent liabilities associated with legal proceedings on our condensed consolidated balance sheet as of September 30, 2017.

Off-balance Sheet Arrangements

During the periods presented, we did not have, and we currently do not have, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Segment Reporting

We view our operations and manage our business as one segment, which is the discovery, research and development of treatments based on our RNAi technology platform.

Item 3. QUANTITATIVE AND QUALITATIVE DISCLOSURE ABOUT MARKET RISK

The primary objectives of our investment activities are to ensure liquidity and to preserve principal while at the same time maximizing the income we receive from our marketable securities without significantly increasing risk. Some of the securities that we invest in may have market risk related to changes in interest rates. As of September 30, 2017, we had cash and cash equivalents and held-to-maturity investments of $75.9 million. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term maturities of our cash and cash equivalents and held-to-maturity investments and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our cash and cash equivalents or held-to-maturity investments. To minimize the risk in the future, we intend to maintain our portfolio of cash and cash equivalents and held-to-maturity investments in a variety of securities, including commercial paper, money market funds and government securities.

Item 4. CONTROLS AND PROCEDURES

Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our periodic and current reports that we file under the Exchange Act with the SEC 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 principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

As of the end of the period covered by this Quarterly Report on Form 10-Q, we carried out an evaluation, under the supervision and with the participation of our management, including the chief executive officer and the chief financial officer, of the effectiveness of the design and operation of our disclosure controls and procedures pursuant to Exchange Act Rule 13a-15. Based upon, and as of the date of, this evaluation, the chief executive officer and the chief financial officer concluded that our disclosure controls and procedures were effective. Accordingly, management believes that the financial statements included in this report fairly present in all material respects our financial condition, results of operations and cash flows for the periods presented.

Changes in Internal Control Over Financial Reporting

We continuously seek to improve the efficiency and effectiveness of our internal controls. This results in refinements to processes throughout the Company. There was no change in our internal control over financial reporting during the quarter ended September 30, 2017, which was identified in connection with our management's evaluation required by Exchange Act Rules 13a-15 and 15d-15 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on the Effectiveness of Controls

Our management, including the chief executive officer and chief financial officer, does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent all error and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within the company have been detected. These inherent limitations include the realities that judgments in decision making can be faulty and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by management override of the control. The design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions. Over time, controls may become inadequate because of changes in conditions, or the degree of compliance with the policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

PART II: OTHER INFORMATION

Item 1. LEGAL PROCEEDINGS

We are not currently a party to or aware of any proceedings that we believe will have, individually or in the aggregate, a material adverse effect on our business, financial condition or results of operations.

On June 10, 2015, Alnylam filed a complaint against the Company in the Superior Court of Middlesex Country, Massachusetts (the "Court"). The complaint alleges misappropriation of confidential, proprietary, and trade secret information, as well as other related claims, in connection with the Company's hiring of a number of former employees of Merck & Co., Inc. ("Merck") and its discussions with Merck regarding the acquisition of its subsidiary, Sirna Therapeutics, Inc. ("Sirna"), which was subsequently acquired by Alnylam. The complaint seeks among other things, unspecified damages, attorneys' fees, and an order permanently enjoining the Company from disclosing or using any of Alnylam's confidential information or trade secrets. The Court has set a trial date of April 23, 2018. This matter has caused us to incur significant legal fees and other costs to defend against this action and will continue to do so through the trial and potentially beyond. We believe, however, that Alnylam's allegations lack merit. In response to the complaint, we filed an answer denying all liability, and we will continue to vigorously defend all claims asserted. We expect that a finding of liability against us is not probable. Accordingly, we cannot reasonably estimate any range of potential future charges, and we have not recorded any accrual for a contingent liability associated with this legal proceeding. However, an unfavorable resolution could potentially have a material adverse effect on our business, financial condition, and results of operations or prospects, potentially delay or limit our ability to use some of our research and development programs, and potentially result in paying monetary damages. Additionally, as we believe Alnylam's suit is without merit and intended only to cause competitive harm, we filed a countersuit in the case against Alnylam for damages, and on August 8, 2017, we filed a complaint in the Federal District court for the District of Massachusetts asserting a federal antitrust claim against Alnylam.

Item 1A. *Risk Factors*

We are providing the following cautionary discussion of risk factors, uncertainties and assumptions that we believe are relevant to our business. These are factors that, individually or in the aggregate, we think could cause our actual results to differ materially from expected and historical results and our forward-looking statements. We note these factors for investors as permitted by Section 21E of the Securities Exchange Act of 1934, as amended, and Section 27A of the Securities Act of 1933, as amended. You should understand that it is not possible to predict or identify all such factors. Consequently, you should not consider this section to be a complete discussion of all potential risks or uncertainties that may substantially impact our business. Moreover, we operate in a competitive and rapidly changing environment. New factors emerge from time to time, and it is not possible to predict the impact of all of these factors on our business, financial condition or results of operations.

Risks Related to Our Business

We will need to raise substantial additional funds to advance development of our product candidates, and we cannot guarantee that we will have sufficient funds available in the future to develop and commercialize our current or future product candidates.

We will need to raise substantial additional funds to expand our development, regulatory, manufacturing, marketing and sales capabilities, whether internally or through other organizations. We have used substantial funds to develop our product candidates and delivery technologies and will require significant funds to conduct further research and development and preclinical testing and clinical trials of our product candidates, to seek regulatory approvals for our product candidates and to manufacture and market products, if any are approved for commercial sale. As of September 30, 2017, we had $75.9 million in cash and cash equivalents and held-to-maturity investments. Based on our current operating plan and liquidity, including the receipt of net proceeds of $69.3 million in connection with the issuance of the Company's Redeemable Convertible Preferred on April 11, 2017 and the receipt of upfront proceeds in connection with the BI Agreement, we believe that our available cash, cash equivalents and held-to-maturity investments will be sufficient to fund our planned level of operations for at least the 12-month period following November 2, 2017. Our future capital requirements and the period for which we expect our existing resources to support our operations may vary significantly from what we expect. Our monthly spending levels vary based on new and ongoing development and corporate activities. Because the length of time and activities associated with successful development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. To execute our business plan, we will need, among other things:

- to obtain the human and financial resources necessary to develop, test, obtain regulatory approval for, manufacture and market our product candidates;
- to build and maintain a strong intellectual property portfolio and avoid infringing intellectual property of third parties;
- to establish and maintain successful licenses, collaborations and alliances;
- to satisfy the requirements of clinical trial protocols, including patient enrollment;
- to establish and demonstrate the clinical efficacy and safety of our product candidates;
- to manage our spending as costs and expenses increase due to preclinical studies and clinical trials, regulatory approvals, manufacturing scale-up and commercialization;
- to obtain additional capital to support and expand our operations; and
- to market our products to achieve acceptance and use by the medical community.

Failure to obtain funding on a timely basis or on acceptable terms would have a negative impact on our financial condition, and we may have to delay, reduce or terminate our research and development programs and preclinical studies or clinical trials, if any, limit strategic opportunities or undergo reductions in our workforce or other corporate restructuring activities. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies or product candidates that we would otherwise pursue on our own. We do not expect to realize revenue from product sales, milestone payments or royalties in the foreseeable future, if at all. Our revenue sources are, and will remain, extremely limited unless and until our product candidates are clinically tested, approved for commercialization and successfully marketed. To date, we have financed our operations primarily through the sale of securities, debt financings, credit and loan facilities and payments received under our collaboration and license agreement with KHK. For example, on April 11, 2017, we issued and sold 700,000 shares of our newly designated Redeemable Convertible Preferred to the Investors in a Private Placement for aggregate gross proceeds of $70.0 million. We will be required to seek additional funding in the future and intend to do so through a combination of public or private equity offerings, debt financings

and research collaborations and license agreements. Our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. For example, a number of factors, including the timing and outcomes of our clinical activities, our status as a smaller reporting company under SEC regulations, our capital structure, which currently consists of common stock and redeemable convertible preferred stock, as well as conditions in the global financial markets, may present significant challenges to accessing the capital markets at a time when we would like or require, and at an increased cost of capital. Additional funds may not be available to us on acceptable terms or at all. If we raise additional funds by issuing equity securities, our stockholders will suffer dilution, and the terms of any financing may adversely affect the rights of our stockholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Debt financing, if available, may involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of equity securities receive any distribution of corporate assets.

We are a biopharmaceutical company with a history of losses, expect to continue to incur significant losses for the foreseeable future and may never achieve or maintain profitability, which could result in a decline in the market value of our common stock.

We are a biopharmaceutical company with a limited operating history focused on the discovery and development of treatments based on the emerging therapeutic modality RNAi, a biological process in which RNA molecules inhibit gene expression. Since our inception in October 2006, we have devoted our resources to the development of DsiRNA molecules and delivery technologies. We have had significant operating losses since our inception. As of September 30, 2017, we had an accumulated deficit of $300.2 million. For the nine months ended September 30, 2017 and for the years ended December 31, 2016, 2015 and 2014, our net loss attributable to common stockholders was $57.3 million, $59.5 million, $62.8 million and $47.9 million, respectively. Substantially all of our operating losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. Our technologies and product candidates are in early stages of development, and we are subject to the risks of failure inherent in the development of product candidates based on novel technologies.

To date, we have generated revenue primarily from the receipt of upfront research funding, license and option exercise fees and preclinical payments under our research collaboration and license agreement with KHK. We have not generated, and do not expect to generate, any revenue from product sales for the foreseeable future, and we expect to continue to incur significant operating losses for the foreseeable future due to the cost of research and development, preclinical studies and clinical trials and the regulatory approval process for product candidates. The amount of future losses is uncertain. Our ability to achieve profitability, if ever, will depend on, among other things, us or our existing collaborators, or any future collaborators, successfully developing product candidates, obtaining regulatory approvals to market and commercialize product candidates, manufacturing any approved products on commercially reasonable terms, establishing a sales and marketing organization or suitable third party alternatives for any approved product and raising sufficient funds to finance business activities. If we or our existing collaborators, or any future collaborators, are unable to develop and commercialize one or more of our product candidates or if sales revenue from any product candidate that receives approval is insufficient, we will not achieve profitability, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expense related to our product candidates or future development programs;
- results of clinical trials, or the addition or termination of clinical trials or funding support by us, our existing collaborators or any future collaborator or licensor;
- the timing of the release of results from any clinical trials conducted by us or our collaborator KHK;
- our execution of any collaboration, licensing or similar arrangement, and the timing of payments we may make or receive under such existing or future arrangements or the termination or modification of any such existing or future arrangements;
- any intellectual property infringement or misappropriation lawsuit or opposition, interference, re-examination, post-grant review, inter partes review, nullification, derivation action, or cancellation proceeding in which we may become involved, including Alnylam's lawsuit alleging misappropriation of confidential information and trade secrets;

- additions and departures of key personnel;
- strategic decisions by us and our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- if any of our product candidates receive regulatory approval, market acceptance and demand for such product candidates;
- if any of our third-party manufacturers fail to execute on our manufacturing requirements;
- regulatory developments affecting our product candidates or those of our competitors;
- disputes concerning patents, proprietary rights, or license and collaboration agreements that negatively impact our receipt of milestone payments or royalties or require us to make significant payments arising from licenses, settlements, adverse judgments or ongoing royalties; and
- changes in general market and economic conditions.

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

Our approach to the discovery and development of innovative therapeutic treatments based on novel technologies is unproven and may not result in marketable products.

We plan to develop subcutaneously delivered RNAi based pharmaceuticals using our GalXC RNAi platform for the treatment of rare diseases involving the liver and for other therapeutic areas involving the liver such as chronic liver diseases, as well as cardiovascular diseases and viral infectious diseases. We believe that product candidates identified with our drug discovery and delivery platform may offer an improved therapeutic approach to small molecules and monoclonal antibodies, as well as several advantages over earlier generation RNAi molecules. However, the scientific research that forms the basis of our efforts to develop product candidates is relatively new. The scientific evidence to support the feasibility of developing therapeutic treatments based on RNAi and GalXC is both preliminary and limited.

Relatively few product candidates based on RNAi have been tested in animals or humans, and a number of clinical trials conducted by other companies using RNAi technologies have not been successful. We may discover that GalXC does not possess certain properties required for a drug to be safe and effective, such as the ability to remain stable in the human body for the period of time required for the drug to reach the target tissue or the ability to cross the cell wall and enter into cells within the target tissue for effective delivery. We currently have only limited data, and no conclusive evidence, to suggest that we can introduce these necessary drug-like properties into GalXC. We may spend substantial funds attempting to introduce these properties and may never succeed in doing so. In addition, product candidates based on GalXC may demonstrate different chemical and pharmacological properties in patients than they do in laboratory studies. Even if product candidates, such as DCR-PHXC, have successful results in animal studies, they may not demonstrate the same chemical and pharmacological properties in humans and may interact with human biological systems in unforeseen, ineffective or harmful ways. As a result, we may never succeed in developing a marketable product, we may not become profitable and the value of our common stock will decline.

Further, the FDA has relatively limited experience with RNAi or GalXC based therapeutics. No regulatory authority has granted approval to any person or entity, including us, to market and commercialize therapeutics using RNAi or GalXC, which may increase the complexity, uncertainty and length of the regulatory approval process for our product candidates. We and our current collaborators, or any future collaborators, may never receive approval to market and commercialize any product candidate. Even if we or a collaborator obtain regulatory approval, the approval may be for disease indications or patient populations that are not as broad as we intended or desired or may require labeling that includes significant use or distribution restrictions or safety warnings. We or a collaborator may be required to perform additional or unanticipated clinical trials to obtain approval or be subject to post-marketing testing requirements to maintain regulatory approval. If our technologies based on GalXC prove to be ineffective, unsafe or commercially unviable, our entire platform and pipeline would have little, if any, value, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

The market may not be receptive to our product candidates based on a novel therapeutic modality, and we may not generate any future revenue from the sale or licensing of product candidates.

Even if approval is obtained for a product candidate, we may not generate or sustain revenue from sales of the product due to numerous factors, including whether the product can be sold at a competitive price and otherwise is accepted in the market. The product candidates that we are developing are based on new technologies and therapeutic approaches. Market participants with significant influence over acceptance of new treatments, such as physicians and third-party payors, may not adopt a treatment based on GalXC technology, and we may not be able to convince the medical community and third-party payors, including health insurers, to accept and use, or to provide favorable coverage or reimbursement for, any product candidates developed by us or our existing collaborator or any future collaborators. Market acceptance of our product candidates will depend on, among other factors:

- the timing of our receipt of any marketing and commercialization approvals;
- the terms of any approvals and the countries in which approvals are obtained;
- the safety and efficacy of our product candidates;
- the prevalence and severity of any adverse side effects associated with our product candidates;
- limitations or warnings contained in any labeling approved by the FDA or other regulatory authority;
- relative convenience and ease of administration of our product candidates;
- the willingness of physicians and patients to accept any new methods of administration;
- the success of our physician education programs;
- the availability of adequate government and third-party payor coverage and reimbursement;
- the pricing of our products, particularly as compared to alternative treatments;
- our ability to compliantly market and sell our products; and
- availability of alternative effective treatments for the disease indications our product candidates are intended to treat and the relative risks, benefits and costs of those treatments.

With our focus on the emerging therapeutic modality RNAi, these risks may increase to the extent the market becomes more competitive or less favorable to this approach. Additional risks apply to any disease indications we pursue which are classified as rare diseases and allow for orphan drug designation by regulatory agencies in major commercial markets, such as the U.S., the EU and Japan. Because of the small patient population for a rare disease, if pricing is not approved or accepted in the market at an appropriate level for an approved product with orphan drug designation, such drug may not generate enough revenue to offset costs of development, manufacturing, marketing and commercialization despite any benefits received from the orphan drug designation, such as market exclusivity, assistance in clinical trial design or a reduction in user fees or tax credits related to development expense. Market size is also a variable in disease indications that are not classified as rare. Our estimates regarding potential market size for any indication may be materially different from what we discover to exist if we ever get to the point of product commercialization, which could result in significant changes in our business plan and have a material adverse effect on our business, financial condition, results of operations and prospects.

If a product candidate that has orphan drug designation subsequently receives the first FDA approval for the indication for that designation, the product candidate is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same product candidate for the same indication, except in very limited circumstances, for seven years. Orphan drug exclusivity, however, could also block the approval of one of our product candidates for seven years if a competitor obtains approval of the same product candidate as defined by the FDA or if our product candidate is determined to be contained within the competitor’s product candidate for the same indication or disease.

As in the U.S., we may apply for designation of a product candidate as an orphan drug for the treatment of a specific indication in the EU before the application for marketing authorization is made. Sponsors of orphan drugs in the EU can enjoy economic and marketing benefits, including up to ten years of market exclusivity for the approved indication unless another applicant can show that its product is safer, more effective or otherwise clinically superior to the orphan-designated product. The respective orphan designation and exclusivity frameworks in the U.S. and in the EU are subject to change, and any such changes may affect our ability to obtain EU or U.S. orphan designations in the future.

Our product candidates are in early stages of development and may fail or suffer delays that materially and adversely affect their commercial viability.

We have no products on the market and all of our product candidates are in early stages of development. Our ability to achieve and sustain profitability depends on obtaining regulatory approvals, including ethics committee approval to conduct clinical trials at particular sites, and successfully commercializing our product candidates, either alone or with third parties, such as our collaborator KHK. Before obtaining regulatory approval for the commercial distribution of our product candidates, we or a collaborator must conduct extensive preclinical tests and clinical trials to demonstrate the safety and efficacy in humans of our product candidates. Preclinical testing and clinical trials are expensive, difficult to design and implement, can take many years to complete and are uncertain as to outcome. The start or end of a clinical study is often delayed or halted due to changing regulatory requirements, manufacturing challenges, required clinical trial administrative actions, slower than anticipated patient enrollment, changing standards of care, availability or prevalence of use of a comparative drug or required prior therapy, clinical outcomes and financial constraints. For instance, delays or difficulties in patient enrollment or difficulties in retaining trial participants can result in increased costs, longer development times or termination of a clinical trial. Clinical trials of a new product candidate require the enrollment of a sufficient number of patients, including patients who are suffering from the disease the product candidate is intended to treat and who meet other eligibility criteria. Rates of patient enrollment are affected by many factors, including the size of the patient population, the eligibility criteria for the clinical trial, the age and condition of the patients, the stage and severity of disease, the nature of the protocol, the proximity of patients to clinical sites and the availability of effective treatments for the relevant disease.

A product candidate can unexpectedly fail at any stage of preclinical and clinical development. The historical failure rate for product candidates is high due to many factors, including scientific feasibility, safety, efficacy and changing standards of medical care. The results from preclinical testing or early clinical trials of a product candidate may not predict the results that will be obtained in later phase clinical trials of the product candidate. We, the FDA, the applicable Institutional Review Board ("IRB"), an independent ethics committee, or other applicable regulatory authorities may suspend clinical trials of a product candidate at any time for various reasons, including a belief that individuals participating in such trials are being exposed to unacceptable health risks or adverse side effects. Similarly, an IRB or ethics committee may suspend a clinical trial at a particular trial site. We may not have the financial resources to continue development of, or to enter into collaborations for, a product candidate if we experience any problems or other unforeseen events that delay or prevent regulatory approval of, or our ability to commercialize, product candidates, including:

- negative or inconclusive results from our clinical trials or the clinical trials of others for product candidates similar to ours, leading to a decision or requirement to conduct additional preclinical testing or clinical trials or abandon a program;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- delays in submitting IND applications or comparable foreign applications or delays or failure in obtaining the necessary approvals from regulators or IRBs to commence a clinical trial, or a suspension or termination of a clinical trial once commenced;
- conditions imposed by the FDA or comparable foreign authorities, such as the European Medicines Agency ("EMA"), regarding the scope or design of our clinical trials;
- delays in enrolling individuals in clinical trials;
- high drop-out rates of study participants;
- inadequate supply or quality of drug product or product candidate components or materials or other supplies necessary for the conduct of our clinical trials;
- greater than anticipated clinical trial costs;
- poor effectiveness of our product candidates during clinical trials;
- unfavorable FDA or other regulatory agency inspection and review of a clinical trial site;
- failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;
- delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular; and
- varying interpretations of data by the FDA and foreign regulatory agencies.

To date, our revenue has been primarily derived from our research collaboration and license agreement with KHK, and we are dependent on KHK for the successful development of product candidates in the collaboration.

In December 2009, we entered into a research collaboration and license agreement with KHK for the research, development and commercialization of DsiRNA molecules and drug delivery technologies for therapeutic targets, primarily in oncology. Under this research collaboration and license agreement, KHK has paid us a total of $17.5 million. During the first two years of the collaboration, we worked together with KHK to optimize KHK's lipid nanoparticles for tumor delivery and to identify DsiRNAs optimized against oncology and KRAS targets. Based on the results of this research, KHK exercised options to advance two separate DsiRNAs into the development stage, including one with a KRAS target. For each product candidate under the research collaboration and license agreement, we have the potential to receive clinical, regulatory and commercialization milestone payments of up to $110.0 million and royalties on net sales of such product candidate. On October 27, 2017, we entered into the BI Agreement to jointly research and develop candidate products using the GalXC platform to target specific disease-linked genes in the hepatocytes for the treatment of chronic liver disease. Under the terms of the BI Agreement, BI agreed to pay us a non-refundable upfront payment of $10 million and we will be eligible to receive up to $191 million in development and commercial milestones and royalty payments on global net sales. The success of our collaboration programs with KHK and BI depends entirely upon the efforts of those collaborators. For example, except for certain co-promotion and profit sharing rights we retain with respect to the KRAS product candidate if it is approved for marketing and commercialization in the U.S., KHK has sole discretion in determining and directing the efforts and resources, including the ability to discontinue all efforts and resources it applies to the development and, if approval is obtained, commercialization and marketing of the product candidates covered by the collaboration. KHK and BI may not be successful in obtaining approvals for the product candidates developed under the collaboration arrangements or in marketing, or arranging for necessary supply, manufacturing or distribution relationships for, any approved products. Under their respective collaboration and license agreements, each of KHK or BI may change its strategic focus or pursue alternative technologies in a manner that results in reduced, delayed or no revenue to us. Each of KHK and BI has a variety of marketed products and product candidates under collaboration with other companies, including some of our competitors, and their own corporate objectives may not be consistent with our interests. If KHK or BI fails to develop, obtain regulatory approval for or ultimately commercialize any product candidate under our collaborations or if either KHK or BI terminate our collaboration, our business, financial condition, results of operations and prospects could be materially and adversely affected. In addition, if we have a dispute or enter into litigation with KHK or BI in the future, it could delay development programs, create uncertainty as to ownership of intellectual property rights, distract management from other business activities and generate substantial expense.

If third parties on which we depend to conduct our preclinical studies, or any future clinical trials, do not perform as contractually required, fail to satisfy regulatory or legal requirements or miss expected deadlines, our development program could be delayed with materially adverse effects on our business, financial condition, results of operations and prospects.

We rely on third party clinical investigators, contract research organizations ("CROs"), clinical data management organizations and consultants to design, conduct, supervise and monitor preclinical studies of our product candidates and will do the same for any clinical trials. Because we rely on third parties and do not have the ability to conduct preclinical studies or clinical trials independently, we have less control over the timing, quality, compliance and other aspects of preclinical studies and clinical trials than we would if we conducted them on our own. These investigators, CROs and consultants are not our employees and we have limited control over the amount of time and resources that they dedicate to our programs. These third parties may have contractual relationships with other entities, some of which may be our competitors, which may draw time and resources from our programs. The third parties with which we contract might not be diligent, careful, compliant, or timely in conducting our preclinical studies or clinical trials, resulting in the preclinical studies or clinical trials being delayed or unsuccessful.

If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of preclinical studies or clinical trials or meet expected deadlines, our clinical development programs could be delayed and otherwise adversely affected. In all events, we are responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the general investigational plan and protocols for the trial as well as applicable laws and regulations. The FDA and certain foreign regulatory authorities, such as the EMA, require preclinical studies to be conducted in accordance with applicable good laboratory practices and clinical trials to be conducted in accordance with applicable FDA regulations and applicable good clinical practices, including requirements for conducting, recording and reporting the results of preclinical studies and clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. Any such event could have a material adverse effect on our business, financial condition, results of operations and prospects.

Because we rely on third party manufacturing and supply partners, our supply of research and development, preclinical studies and clinical trial materials may become limited or interrupted or may not be of satisfactory quantity or quality.

We rely on third party supply and manufacturing companies and organizations to supply the materials, components and manufacturing services for our research and development, preclinical study and clinical trial drug supplies.

We do not own or lease manufacturing facilities or supply sources for such components and materials. Our manufacturing requirements include oligonucleotides and custom amidites, some of which we procure from a single source supplier on a purchase order basis. In addition, for each product candidate we contract with only one manufacturer for the formulation and filling of drug product. There can be no assurance that our supply of research and development, preclinical study and clinical trial drugs and other materials will not be limited, interrupted, restricted in certain geographic regions or of satisfactory quality or continue to be available at acceptable prices. In particular, any replacement of our drug substance manufacturer could require significant effort and expertise because there may be a limited number of qualified replacements.

If we are at any time unable to provide an uninterrupted supply of our product candidates or, following regulatory approval, any products to patients, we may lose patients, physicians may elect to utilize competing therapeutics instead of our products, and our clinical trials may be adversely affected, which could materially and adversely affect our clinical trial outcome.

The manufacturing process for a product candidate is subject to FDA and foreign regulatory authority review. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as current good manufacturing practices ("cGMP"). In the event that any of our suppliers or manufacturers fails to comply with such requirements or to perform its obligations regarding quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may experience shortages resulting in delayed shipments, supply constraints and/or stock-outs of our products, be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills or technology to another third party and a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

We expect to continue to rely on third party manufacturers if we receive regulatory approval for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. If we are unable to obtain or maintain third-party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third party's failure to execute on our manufacturing requirements could adversely affect our business in a number of ways, including:

- an inability to initiate or continue preclinical studies or clinical trials of product candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for product candidates;
- loss of the cooperation of a collaborator;
- subjecting manufacturing facilities of our product candidates to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of our product candidates; and
- in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products.

We may not successfully engage in strategic transactions, including any additional collaborations we seek, which could adversely affect our ability to develop and commercialize product candidates, impact our cash position, increase our expense and present significant distractions to our management.

From time to time, we may consider strategic transactions, such as collaborations, acquisitions of companies, asset purchases and out- or in-licensing of product candidates or technologies. In particular, in addition to our current arrangements with KHK, COH, Carnegie and PBL, we will evaluate and, if strategically attractive, seek to enter into additional collaborations, including with major biotechnology or pharmaceutical companies. The competition for collaborators is intense, and the negotiation process is time-consuming and complex. Any new collaboration may be on terms that are not optimal for us, and we may be unable to maintain any new or existing collaboration if, for example, development or approval of a product candidate is delayed, sales of an approved product do not meet expectations or the collaborator terminates the collaboration. Any such collaboration, or other strategic transaction, may require us to incur non-recurring or other charges, increase our near- and long-term expenditures and pose significant integration or implementation challenges or disrupt our management or business. These transactions entail numerous operational and financial risks, including exposure to unknown liabilities, disruption of our business and diversion of our management's time and attention in order to manage a collaboration or develop acquired products, product candidates or technologies, incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs, higher than expected collaboration, acquisition or integration costs, write-downs of assets or goodwill or impairment charges, increased amortization expenses, difficulty and cost in facilitating the collaboration or combining the operations and personnel of any acquired business, impairment of relationships with key suppliers, manufacturers or customers of any acquired business due to changes in management and ownership and the inability to retain key employees of any acquired business. Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks and have a material adverse effect on our business, results of operations, financial condition and prospects. Conversely, any failure to enter any collaboration or other strategic transaction that would be beneficial to us could delay the development and potential commercialization of our product candidates and have a negative impact on the competitiveness of any product candidate that reaches market.

We face competition from entities that have developed or may develop product candidates for our target disease indications, including companies developing novel treatments and technology platforms based on modalities and technology similar to ours. If these companies develop technologies or product candidates more rapidly than we do or their technologies, including delivery technologies, are more effective, our ability to develop and successfully commercialize product candidates may be adversely affected.

The development and commercialization of drugs is highly competitive. We compete with a variety of multinational pharmaceutical companies and specialized biotechnology companies, as well as technology being developed at universities and other research institutions Our competitors have developed, are developing or may develop product candidates and processes competitive with our product candidates, some of which may become commercially available before any of our product candidates. Competitive therapeutic treatments include those that have already been approved and accepted by the medical community and any new treatments that enter the market. We are aware of many companies that are working in the field of RNAi therapeutics, including a major pharmaceutical company, Takeda Pharmaceutical Company Limited, and biopharmaceutical companies such as Alnylam, which acquired Sirna from Merck in March 2014, Arbutus, Arrowhead, Silence Therapeutics plc, RXi Pharmaceuticals Corporation, Quark Pharmaceuticals, Inc., Wave Life Sciences, Benitec Biopharma Limited and Arcturus Therapeutics. In particular, Arrowhead holds a non-exclusive license to the same patent rights of COH and Integrated Data Technologies, Inc. ("IDT") as we are licensed under our license agreement with COH. As a result, we cannot rely on those patent rights to prevent Arrowhead or third parties working with Arrowhead from developing, marketing and selling products that compete directly with some of our product candidates. In March 2015, Arrowhead announced the acquisition of Novartis' RNAi research and development portfolio and associated assets. The acquisition includes assignment of certain intellectual property owned or controlled by Novartis, including access to non-delivery Alnylam RNAi IP for 30 targets, and three preclinical RNAi candidates for which Novartis has developed varying amounts of preclinical data. We believe that a significant number of products are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may try to develop product candidates.

We also compete with companies working to develop antisense and other RNA-based drugs. Like RNAi therapeutics, antisense drugs target mRNA with the objective of suppressing the activity of specific genes. The development of antisense drugs is more advanced than that of RNAi therapeutics, and antisense technology may become the preferred technology for products that target mRNAs. Significant competition also exists from companies such as Alnylam and Arrowhead to discover and develop safe and effective means to deliver therapeutic RNAi molecules, such as DsiRNAs, to the relevant cell and tissue types.

Many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales and supply resources or experience than we have. If we successfully obtain approval for any product candidate, we will face competition based on many different factors, including safety and effectiveness, ease with which our products can be administered and the extent to which patients and physicians accept relatively new routes of administration, timing and scope of regulatory approvals, availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position of our products. Competing products could present superior treatment alternatives, including by being more effective, safer, less expensive or marketed and sold more effectively than any products we may develop. Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. Competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan.

Any inability to attract and retain qualified key management and technical personnel would impair our ability to implement our business plan.

Our success largely depends on the continued service of key management and other specialized personnel, including: Douglas M. Fambrough, III, Ph.D., our chief executive officer; Bob D. Brown, Ph.D., our chief scientific officer; Ralf Rosskamp, M.D., our chief medical officer; John B. Green, our chief financial officer; and James B. Weissman, our chief business officer. The loss of one or more members of our management team or other key employees or advisors could delay our research and development programs and materially harm our business, financial condition, results of operations and prospects. The relationships that our key managers have cultivated within our industry make us particularly dependent upon their continued employment with us. We are dependent on the continued service of our technical personnel because of the highly complex nature of our product candidates and technologies and the specialized nature of the regulatory approval process. Because our management team and key employees are not obligated to provide us with continued service, they could terminate their employment with us at any time without penalty. We do not maintain key person life insurance policies on any of our management team members or key employees. Our future success will depend in large part on our continued ability to attract and retain other highly qualified scientific, technical and management personnel, as well as personnel with expertise in clinical testing, manufacturing, governmental regulation and commercialization. We face competition for personnel from other companies, universities, public and private research institutions, government entities and other organizations.

If our product candidates advance into clinical trials, we may experience difficulties in managing our growth and expanding our operations.

We have limited experience in drug development and very limited experience with clinical trials of product candidates. As our product candidates enter and advance through preclinical studies and any clinical trials, we will need to expand our development, regulatory and manufacturing capabilities or contract with other organizations to provide these capabilities for us. In the future, we expect to have to manage additional relationships with collaborators, suppliers and other organizations. Our ability to manage our operations and future growth will require us to continue to improve our operational, financial and management controls, reporting systems and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls.

If any of our product candidates are approved for marketing and commercialization and we are unable to develop sales, marketing and distribution capabilities on our own or enter into agreements with third parties to perform these functions on acceptable terms, we will be unable to successfully commercialize any such future products.

We currently have no sales, marketing or distribution capabilities or experience. If any of our product candidates are approved, we will need to develop internal sales, marketing and distribution capabilities to commercialize such products, which would be expensive and time-consuming, or enter into collaborations with third parties to perform these services. If we decide to market our products directly, we will need to commit significant financial, legal and managerial resources to develop a marketing and sales force with technical expertise and supporting distribution, administration and compliance capabilities. If we rely on third parties with such capabilities to market our approved products or decide to co-promote products with collaborators, we will need to establish and maintain marketing and distribution arrangements with third parties, and there can be no assurance that we will be able to enter into such arrangements on acceptable, compliant terms, or at all. In entering into third-party marketing or distribution arrangements, any revenue we receive will depend upon the efforts of the third parties and there can be no assurance that such third parties will establish adequate sales and distribution capabilities or be successful in gaining market acceptance of any approved product. If we are not successful in commercializing any product approved in the future, either on our own or through third parties, our business, financial condition, results of operations and prospects could be materially and adversely affected.

If we fail to comply with U.S. and foreign regulatory requirements, regulatory authorities could limit or withdraw any marketing or commercialization approvals we may receive and subject us to other penalties that could materially harm our business.

The Company, our product candidates, our suppliers, and our contract manufacturers, distributors, and contract testing laboratories are subject to extensive regulation by governmental authorities in the EU, the United States, and other countries, with the regulations differing from country to country.

Even if we receive marketing and commercialization approval of a product candidate, we and our third-party services providers will be subject to continuing regulatory requirements, including a broad array of regulations related to establishment registration and product listing, manufacturing processes, risk management measures, quality and pharmacovigilance systems, post-approval clinical studies, labeling, advertising and promotional activities, record keeping, distribution, adverse event reporting, import and export of pharmaceutical products, pricing, sales and marketing, and fraud and abuse requirements. We are required to submit safety and other post market information and reports and are subject to continuing regulatory review, including in relation to adverse patient experiences with the product and clinical results that are reported after a product is made commercially available, both in the U.S. and any foreign jurisdiction in which we seek regulatory approval. The FDA and certain foreign regulatory authorities, such as the EMA, have significant post-market authority, including the authority to require labeling changes based on new safety information and to require post-market studies or clinical trials to evaluate safety risks related to the use of a product or to require withdrawal of the product from the market. The FDA also has the authority to require a risk evaluation and mitigation strategy ("REMS") plan after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug. The EMA now routinely requires risk management plans ("RMPs") as part of the marketing authorization application process, and such plans must be continually modified and updated throughout the lifetime of the product as new information becomes available. In addition, the relevant governmental authority of any EU member state can request an RMP whenever there is a concern about a risk affecting the benefit risk balance of the product. The manufacturer and manufacturing facilities we use to make a future product, if any, will also be subject to periodic review and inspection by the FDA and other regulatory agencies, including for continued compliance with cGMP requirements. The discovery of any new or previously unknown problems with our third-party manufacturers, manufacturing processes or facilities may result in restrictions on the product, manufacturer or facility, including withdrawal of the product from the market. If we rely on third-party manufacturers, we will not have control over compliance with applicable rules and regulations by such manufacturers. Any product promotion and advertising will also be subject to regulatory requirements and continuing regulatory review. If we or our collaborators, manufacturers or service providers fail to comply with applicable continuing regulatory requirements in the U.S. or foreign jurisdictions in which we seek to market our products, we or they may be subject to, among other things, fines, warning and untitled letters, clinical holds, delay or refusal by the FDA or foreign regulatory authorities to approve pending applications or supplements to approved applications, suspension, refusal to renew or withdrawal of regulatory approval, product recalls, seizures or administrative detention of products, refusal to permit the import or export of products, operating restrictions, inability to participate in government programs including Medicare and Medicaid, and total or partial suspension of production or distribution, injunction, restitution, disgorgement, debarment, civil penalties and criminal prosecution.

We have a subsidiary physically located in the United Kingdom ("UK"), which we established in order to allow us to conduct clinical trials in EU member states. On June 23, 2016, the UK held a referendum in which voters approved an exit from the EU, commonly referred to as "Brexit." The withdrawal of the UK from the EU will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the UK provides a notice of withdrawal pursuant to the EU Treaty. On March 29, 2017, the Prime Minister of the UK delivered a formal notice of withdrawal to the EU. On May 22, 2017, the Council of the EU (the "Council"), adopted a decision authorizing the opening of Brexit negotiations with the UK and formally nominated the European Commission as EU negotiator. The Council also adopted negotiating directives for the talks. It appears likely that the UK's withdrawal from the EU will involve a process of lengthy negotiations between the UK and EU member states to determine the future terms of the UK's relationship with the EU. This could lead to a period of uncertainty and could impact our regulatory process in Europe, as well as require us to close our subsidiary in the UK and establish a new subsidiary elsewhere in the EU.

Price controls imposed in foreign markets and downward pricing pressure in the U.S. may adversely affect our future profitability.

In some countries, particularly member states of the EU, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a product. In addition, in the U.S. and elsewhere, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing and reimbursement negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we or our collaborators may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our RNAi therapeutic candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of any product candidate approved for marketing is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, financial condition, results of operations or prospects could be adversely affected.

Our business entails a significant risk of product liability and our ability to obtain sufficient insurance coverage could harm our business, financial condition, results of operations or prospects.

Our business exposes us to significant product liability risks inherent in the development, testing, manufacturing and marketing of therapeutic treatments. Product liability claims could delay or prevent completion of our development programs. If we succeed in marketing products, such claims could result in an investigation by certain regulatory authorities, such as the FDA or foreign regulatory authorities, of the safety and effectiveness of our products, our manufacturing processes and facilities or our marketing programs and potentially a recall of our products or more serious enforcement action, limitations on the approved indications for which they may be used or suspension or withdrawal of approvals. Regardless of the merits or eventual outcome, liability claims may also result in decreased demand for our products, injury to our reputation, costs to defend related litigation, a diversion of management's time and our resources, substantial monetary awards to clinical trial participants or patients and a decline in our stock price. We currently have product liability insurance that we believe is appropriate for our stage of development and may need to obtain higher levels prior to marketing any of our product candidates. Any insurance we have or may obtain may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could have a material adverse effect on our business.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include, but is not limited to, intentional failures to comply with FDA or U.S. health care laws and regulations or applicable laws, regulations, guidance or codes of conduct set by foreign governmental authorities or self-regulatory industry organizations, provide accurate information to any governmental authorities such as the FDA, comply with manufacturing standards we may establish, comply with federal and state healthcare fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws, regulations, guidance and codes of conduct intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws, regulations, guidance and codes of conduct may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive program, health care professional, and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions, including debarment or disqualification of those employees from participation in FDA regulated activities, and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, regulations, guidance or codes of conduct. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines, exclusion from government programs, or other sanctions.

Our internal computer systems, or those of third parties with which we do business, including our CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs or the theft of Company or patient confidential information.

Despite the implementation of security measures, our internal computer systems and those of third parties with which we do business, including our CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such events could cause interruptions of our operations. For instance, the loss of preclinical data or data from any future clinical trial involving our product candidates could result in delays in our development and regulatory filing efforts and significantly increase our costs. Certain data breaches must also be reported to affected individuals and the government, and in some cases to the media, under provisions of the U.S. federal Health Insurance Portability and Accountability Act ("HIPAA"), as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH"), other U.S. federal and state law, and requirements of non-U.S. jurisdictions, including the European Union Data Protection Directive, and financial penalties may also apply. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data, or inappropriate disclosure of confidential or proprietary information of the Company or patients, we could incur liability and the development of our product candidates could be delayed.

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 research, development and manufacturing involve the use of hazardous materials and various chemicals. We maintain quantities of various flammable and toxic chemicals in our facilities in Cambridge, Massachusetts, that are required for our research, development and manufacturing activities. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. We believe our procedures for storing, handling and disposing these materials in our Cambridge facilities comply with the relevant guidelines of Cambridge, the Commonwealth of Massachusetts and the Occupational Safety and Health Administration of the U.S. Department of Labor. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards mandated by applicable regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. If an accident occurs, we could be held liable for resulting damages, which could be substantial. We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood-borne pathogens and the handling of animals and biohazardous materials. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of these materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological or hazardous materials. Additional federal, state and local laws and regulations affecting our operations may be adopted in the future. We may incur substantial costs to comply with, and substantial fines or penalties if we violate any of these laws or regulations.

Our information technology systems could face serious disruptions that could adversely affect our business.

Our information technology and other internal infrastructure systems, including corporate firewalls, servers, leased lines and connection to the Internet, face the risk of systemic failure that could disrupt our operations. A significant disruption in the availability of our information technology and other internal infrastructure systems could cause interruptions in our collaborations and delays in our research and development work.

Our current operations are concentrated in one location and any events affecting this location may have material adverse consequences.

Our current operations are located in our facilities situated in Cambridge. Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, power shortage, telecommunication failure or other natural or manmade accidents or incidents that prevent us from fully utilizing the facilities, may have a material adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our product candidates or interruption of our business operations. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Any business interruption may have a material adverse effect on our business, financial position, results of operations and prospects.

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

We have incurred substantial losses during our history, do not expect to become profitable for the foreseeable future and may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. We may be unable to use these losses to offset income before such unused losses expire. Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50 percentage point change by value in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be further limited. We have not performed an analysis on whether we have experienced any ownership changes in the past. It is possible that we have experienced an ownership change, including pursuant to the initial public offering of our common stock, which closed on February 4, 2014, and our net operating losses are subject to such limitation. Additionally, we may experience an ownership change upon conversion of our Redeemable Convertible Preferred to common stock. As of December 31, 2016, we had significant U.S. federal and Massachusetts net operating loss carryforwards. Any limit on these loss carryforwards if we have or do experience an ownership change could have an adverse effect on our business, financial position, results of operations and prospects.

The investment of our cash and cash equivalents and held-to-maturity investments is subject to risks which may cause losses and affect the liquidity of these investments.

As of September 30, 2017, we had $75.9 million in cash and cash equivalents and held-to-maturity investments. We historically have invested substantially all of our available cash and cash equivalents in corporate bonds, commercial paper, securities issued by the U.S. government, certificates of deposit and money market funds meeting the criteria of our investment policy, which is focused on the preservation of our capital. These investments are subject to general credit, liquidity, market and interest rate risks. For example, the impact of U.S. sub-prime mortgage defaults in recent years affected various sectors of the financial markets and caused credit and liquidity issues. We may realize losses in the fair value of these investments or a complete loss of these investments, which would have a negative effect on our condensed consolidated financial statements.

In addition, should our investments cease paying or reduce the amount of interest paid to us, our interest income would suffer. The market risks associated with our investment portfolio may have an adverse effect on our results of operations, liquidity and financial condition.

Changes in accounting rules and regulations, or interpretations thereof, could result in unfavorable accounting charges or require us to change our compensation policies.

Accounting methods and policies for biopharmaceutical companies, including policies governing revenue recognition, research and development and related expenses and accounting for stock-based compensation, are subject to review, interpretation and guidance from our auditors and relevant accounting authorities, including the U.S. Securities and Exchange Commission. Changes to accounting methods or policies, or interpretations thereof, may require us to reclassify, restate or otherwise change or revise our consolidated financial statements, including those contained in our Annual Reports on Form 10-K.

Risks Related to Intellectual Property

If we are not able to obtain and enforce patent protection for our technologies or product candidates, development and commercialization of our product candidates may be adversely affected.

Our success depends in part on our ability to obtain and maintain patents and other forms of intellectual property rights, including in-licenses of intellectual property rights of others, for our product candidates, methods used to manufacture our product candidates and methods for treating patients using our product candidates, as well as our ability to preserve our trade secrets, to prevent third parties from infringing upon our proprietary rights and to operate without infringing upon the proprietary rights of others. As of November 1, 2017, our worldwide patent estate, not including the patents and patent applications that we have licensed from third parties, included over 20 issued patents or allowed patent applications and over 100 pending patent applications supporting commercial development of our RNAi molecules and delivery technologies. We may not be able to apply for patents on certain aspects of our product candidates or delivery technologies in a timely fashion or at all. Our existing issued and granted patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing products and technology. There is no guarantee that any of our pending patent applications will result in issued or granted patents, that any of our issued or granted patents will not later be found to be invalid or unenforceable or that any issued or granted patents will include claims that are sufficiently

broad to cover our product candidates or delivery technologies or to provide meaningful protection from our competitors. Moreover, the patent position of biotechnology and pharmaceutical companies can be highly uncertain because it involves complex legal and factual questions. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our current and future proprietary technology and product candidates are covered by valid and enforceable patents or are effectively maintained as trade secrets. If third parties disclose or misappropriate our proprietary rights, it may materially and adversely impact our position in the market.

The U.S. Patent and Trademark Office ("USPTO") and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case. The standards applied by the USPTO and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and pharmaceutical patents. As such, we do not know the degree of future protection that we will have on our proprietary products and technology. While we will endeavor to protect our product candidates with intellectual property rights such as patents, as appropriate, the process of obtaining patents is time-consuming, expensive and sometimes unpredictable.

In addition, there are numerous recent changes to the patent laws and proposed changes to the rules of the USPTO which may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, the Leahy-Smith America Invents Act enacted in 2011 involves significant changes in patent legislation. The U.S. Supreme Court has ruled on several patent cases in recent years, some of which cases either narrow the scope of patent protection available in certain circumstances or weaken the rights of patent owners in certain situations. The 2013 decision by the U.S. Supreme Court in *Association for Molecular Pathology v. Myriad Genetics, Inc.* precludes a claim to a nucleic acid having a stated nucleotide sequence which is identical to a sequence found in nature and unmodified. We currently are not aware of an immediate impact of this decision on our patents or patent applications because we are developing nucleic acid products that are not found in nature. However, this decision has yet to be clearly interpreted by courts and by the USPTO. We cannot assure you that the interpretations of this decision or subsequent rulings will not adversely impact our patents or patent applications. 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 U.S. Congress, the federal courts and the USPTO, the laws and regulations governing U.S. 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.

Once granted, patents may remain open to opposition, interference, re-examination, post-grant review, inter partes review, nullification or derivation action in court or before patent offices or similar proceedings for a given period before or after allowance or grant, during which time third parties can raise objections against such initial grant. In the course of such proceedings, which may continue for a protracted period of time, the patent owner may be compelled to limit the scope of the allowed or granted claims thus attacked, or may lose the allowed or granted claims altogether. Our patent risks include that:

- others may, or may be able to, make, use or sell compounds that are the same as or similar to our product candidates but that are not covered by the claims of the patents that we own or license;
- we or our licensors, collaborators or any future collaborators may not be the first to file patent applications covering certain aspects of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- a third party may challenge our patents and, if challenged, a court may not hold that our patents are valid, enforceable and infringed;
- a third party may challenge our patents in various patent offices and, if challenged, we may be compelled to limit the scope of our allowed or granted claims or lose the allowed or granted claims altogether;
- any issued patents that we own or have licensed from others may not provide us with any competitive advantages, or may be challenged by third parties;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others could harm our business; and

- our competitors could conduct research and development activities in countries where we will not have enforceable patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets.

Intellectual property rights of third parties could adversely affect our ability to commercialize our product candidates, and we might be required to litigate or obtain licenses from third parties in order to develop or market our product candidates. Such litigation could be costly and licenses may be unavailable on commercially reasonable terms.

Research and development of RNAi-based therapeutics and other oligonucleotide-based therapeutics has resulted in many patents and patent applications from organizations and individuals seeking to obtain patent protection in the field. Our efforts are based on RNAi technology that we have licensed and that we have developed internally and own. We have chosen this approach to increase our likelihood of technical success and our freedom to operate. We have obtained grants and issuances of RNAi-based patents and have licensed other patents from third parties on exclusive and non-exclusive bases. The issued patents and pending patent applications in the U.S. and in key markets around the world that we own or license claim many different methods, compositions and processes relating to the discovery, development, manufacture and commercialization of RNAi therapeutics. Specifically, we own and have licensed a portfolio of patents, patent applications and other intellectual property covering: (1) certain aspects of the structure and uses of RNAi molecules, including their manufacture and use as therapeutics, and RNAi-related mechanisms, (2) chemical modifications to RNAi molecules that improve their properties and suitability for therapeutic uses, (3) RNAi molecules directed to specific gene sequences and drug targets as treatments for particular diseases and (4) delivery technologies, such as in the field of lipid nanoparticles and lipid nanoparticle formulation, and chemical modifications such as conjugation to targeting moieties.

The RNAi-related intellectual property landscape, including patent applications in prosecution where no definitive claims have yet issued, is still evolving, and it is difficult to conclusively assess our freedom to operate. Other companies are pursuing patent applications and possess issued patents broadly directed to RNAi compositions, methods of making and using RNAi and to RNAi-related delivery and modification technologies. Our competitive position may suffer if patents issued to third parties cover our products, or our manufacture or uses relevant to our commercialization plans. In such cases, we may not be in a position to commercialize products unless we enter into a license agreement with the intellectual property right holder, if available, on commercially reasonable terms or successfully pursue litigation, opposition, interference, re-examination, post-grant review, inter partes review, nullification, derivation action, or cancellation proceeding to limit, nullify or invalidate the third party intellectual property right concerned. Even if we are successful in limiting, nullifying, or invalidating third party intellectual property rights through such proceedings, we may incur substantial costs and could require significant time and attention of our personnel.

While we believe our intellectual property allows us to pursue our current development programs, the biological process of RNAi is a natural process and cannot be patented. Several companies in the space are pursuing alternate methods to exploit this phenomenon and have built their intellectual property around these methods. For example, Alnylam controls three patent families containing both pending patent applications and issued patents (e.g., U.S. Patent Numbers 8,853,384 and 9,074,213, and European Patent EP 1 352 061 B1) that pertain to RNAi. These are referred to in their corporate literature as the “Tuschl family” (e.g. patents and applications claiming priority to WO2002/044321, filed November 29, 2001, and their priority filings) and the “Kreutzer-Limmer family” (e.g. patents and applications claiming priority to WO 2002/044895, filed January 29, 2000, WO 2002/055693, filed January 9, 2002, and their priority filings). Both families contain patent applications still in prosecution, with the applicants actively seeking to extend the reach of this intellectual property in ways that might strategically impact our business. Additional areas of intellectual property pursued by Alnylam and others include oligonucleotide delivery-related technologies (such as conjugation to targeting moieties) and oligonucleotides directed to specific gene targets. In addition, Silence Therapeutics owns patents directed to certain chemical modifications of RNAi molecules, including U.S. Patent Number 9,222,092, with a priority date of August 5, 2002.

Patent applications in the U.S. and elsewhere are generally published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our product candidates or platform technology could have been filed by others without our knowledge. Additionally, pending claims in patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our platform technologies, our product candidates or the use of our product candidates. Third party intellectual property right holders may also bring patent infringement claims against us. No such patent infringement actions have been brought against us. We cannot guarantee that we will be able to successfully settle or otherwise resolve any future infringement claims. If we are unable to successfully settle future claims on terms acceptable to us, we may be required to engage in or continue costly, unpredictable and time-consuming litigation and may be prevented from or experience substantial delays in marketing our products. If we fail in any such dispute, in addition to being forced to pay damages, we may be temporarily or permanently prohibited from commercializing any of our product

candidates that are held to be infringing. We might also be forced to redesign product candidates so that we no longer infringe the third party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

As the field of RNAi therapeutics matures, patent applications are being processed by national patent offices around the world. There is uncertainty about which patents will issue, and, if they do, as to when, to whom, and with what claims. It is likely that there will be significant litigation in the courts and other proceedings, such as interference, re-examination, opposition, post-grant review, inter partes review, nullification, derivation action, or cancellation proceedings, in various patent offices relating to patent rights in the RNAi therapeutics field. In many cases, the possibility of appeal or opposition exists for either us or our opponents, and it may be years before final, unappealable rulings are made with respect to these patents in certain jurisdictions. The timing and outcome of these and other proceedings is uncertain and may adversely affect our business if we are not successful in defending the patentability and scope of our pending and issued patent claims or if third parties are successful in obtaining claims that cover our RNAi technology or any of our product candidates. In addition, third parties may attempt to invalidate our intellectual property rights. Even if our rights are not directly challenged, disputes could lead to the weakening of our intellectual property rights. Our defense against any attempt by third parties to circumvent or invalidate our intellectual property rights could be costly to us, could require significant time and attention of our management and could have a material adverse effect on our business and our ability to successfully compete in the field of RNAi therapeutics.

There are many issued and pending patents that claim aspects of oligonucleotide chemistry and modifications that we may need to apply to our therapeutic candidates. There are also many issued patents that claim targeting genes or portions of genes that may be relevant for drugs we wish to develop. Thus, it is possible that one or more organizations will hold patent rights to which we will need a license. If those organizations refuse to grant us a license to such patent rights on reasonable terms, we may be unable to market products or perform research and development or other activities covered by these patents.

We license patent rights from third-party owners or licensees. If such owners or licensees do not properly or successfully obtain, maintain or enforce the patents underlying such licenses, or if they retain or license to others any competing rights, our competitive position and business prospects may be adversely affected.

We do, and will continue to, rely on intellectual property rights licensed from third parties to protect our technology. We are a party to a number of licenses that give us rights to third-party intellectual property that is necessary or useful for our business. In particular, we have a license from COH (on behalf of itself and IDT) to certain patent rights, which provide platform intellectual property for research and development of DsiRNA molecules employed in our collaborative programs with KHK. Pursuant to this agreement, we have a worldwide license from COH (subject to the pre-existing non-exclusive license) for the exploitation of key intellectual property rights in this respect, and COH and IDT retain ownership of the patents and patent applications to which we are licensed under the agreement. We also may license additional third-party intellectual property in the future. Our success will depend in part on the ability of our licensors to obtain, maintain and enforce patent protection for our licensed intellectual property, in particular, those patents to which we have secured exclusive rights. Our licensors may not successfully prosecute the patent applications licensed to us. Even if patents issue or are granted, our licensors may fail to maintain these patents, may determine not to pursue litigation against other companies that are infringing these patents, or may pursue litigation less aggressively than we would. Further, we may not obtain exclusive rights, which would allow for third parties to develop competing products. Without protection for, or exclusive right to, the intellectual property we license, other companies might be able to offer substantially identical products for sale, which could adversely affect our competitive business position and harm our business prospects. In addition, we sublicense our rights under our third-party licenses to KHK and may sublicense such rights to current or future collaborators. Any impairment of these sublicensed rights could result in reduced revenue under our collaboration agreement with KHK or result in termination of an agreement by one or more of our collaborators or any future strategic partners.

Certain third parties may also have rights in the patents related to DsiRNA included in the license granted to us by COH, including the core DsiRNA patent (U.S. 8,084,599), which could allow them to develop, market and sell product candidates in competition with ours.

To the extent that we do not have exclusive rights in the patents covered by the license granted to us by COH, we cannot prevent third parties from developing DsiRNA based product candidates in competition with certain of our GalXC products. Prior to entering into the license with us, COH had entered into a non-exclusive license with a third party with respect to such patent rights to manufacture, use, import, offer for sale and sell products covered by the licensed patent rights for the treatment or prevention of disease in humans (excluding viruses and delivery of products into the eye or ear). While we believe that such non-exclusive license has been terminated, COH has informed us that a sublicensee to that non-exclusive license was permitted to enter into an equivalent non-exclusive license which, to our knowledge, is subsisting with Arrowhead, as successor to the non-exclusive license holder. As successor to the non-exclusive license holder, we believe that Arrowhead has substantially similar access to the same patent rights related to technology granted to us under our license with COH. Arrowhead is developing RNA-based therapeutics for the treatment of diseases of the liver, which may directly compete with our product candidates. In addition, the U.S. government has certain rights to the inventions covered by the patent rights and COH, as an academic research and medical center, has the right to practice the licensed patent rights for educational, research and clinical uses. If Arrowhead or another party develops, manufactures, markets and sells any product covered by the same patent rights and technologies that compete with ours, it could significantly undercut the value of any of our product candidates, which would materially and adversely affect our revenue, financial condition and results of operations.

We may be unable to protect our intellectual property rights throughout the world.

Obtaining a valid and enforceable issued or granted patent covering our technology in the U.S. and worldwide can be extremely costly. In jurisdictions where we have not obtained patent protection, competitors may use our technology to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but where it is more difficult to enforce a patent as compared to the U.S. We also may face competition in jurisdictions where we do not have issued or granted patents or where our issued or granted patent claims or other intellectual property rights are not sufficient to prevent competitor activities in these jurisdictions. The legal systems of certain countries, particularly certain developing countries, make it difficult to enforce patents and such countries may not recognize other types of intellectual property protection, particularly that relating to biopharmaceuticals. This could make it difficult for us to prevent the infringement of our patents or marketing of competing products in violation of our proprietary rights generally in certain jurisdictions. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

We generally file a provisional patent application first (a priority filing) at the USPTO. A U.S. utility application and international application under the Patent Cooperation Treaty (“PCT”) are usually filed within twelve months after the priority filing. Based on the PCT filing, national and regional patent applications may be filed in the EU, Japan, Australia and Canada and, depending on the individual case, also in any or all of, inter alia, China, India, South Korea, Singapore, Taiwan and South Africa. We have so far not filed for patent protection in all national and regional jurisdictions where such protection may be available. In addition, we may decide to abandon national and regional patent applications before grant. Finally, the grant proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications might be refused in some jurisdictions, while granted by others. Depending on the country, various scopes of patent protection may be granted on the same product candidate or technology.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws in the U.S., and many companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition from others in those jurisdictions. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position in the relevant jurisdiction may be impaired and our business and results of operations may be adversely affected.

We, our licensors or existing or future collaborators may become subject to third party claims or litigation alleging infringement of patents or other proprietary rights or seeking to invalidate patents or other proprietary rights, and we may need to resort to litigation to protect or enforce our patents or other proprietary rights, all of which could be costly, time consuming, delay or prevent the development and commercialization of our product candidates, or put our patents and other proprietary rights at risk.

We, our licensors or existing or future collaborators may be subject to third-party claims for infringement or misappropriation of patent or other proprietary rights. We are generally obligated under our license or collaboration agreements to indemnify and hold harmless our licensors or collaborators for damages arising from intellectual property infringement by us. If we, our licensors or existing or future collaborators are found to infringe a third party patent or other intellectual property rights, we could be required to pay damages, potentially including treble damages, if we are found to have willfully infringed. In addition, we, our licensors or existing or future collaborators may choose to seek, or be required to seek, a license from a third party, which may not be available on acceptable terms, if at all. Even if a license can be obtained on acceptable terms, the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. If we fail to obtain a required license, we, our licensors or existing or future collaborators may be unable to effectively market product candidates based on our technology, which could limit our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. In addition, we may find it necessary to pursue claims or initiate lawsuits to protect or enforce our patent or other intellectual property rights. The cost to us in defending or initiating any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in our favor, could be substantial, and litigation would divert our management's attention. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations.

If we were to initiate legal proceedings against a third party to enforce a patent covering one of our products or our technology, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during patent prosecution. The outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during patent prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one or more of our products or certain aspects of our platform technology. Such a loss of patent protection could have a material adverse impact on our business. Patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without legally infringing our patents or other intellectual property rights.

If we fail to comply with our obligations under any license, collaboration or other agreements, we may be required to pay damages and could lose intellectual property rights that are necessary for developing and protecting our product candidates and delivery technologies or we could lose certain rights to grant sublicenses.

Our current licenses impose, and any future licenses we enter into are likely to impose, various development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement, and other obligations on us. If we breach any of these obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages and the licensor may have the right to terminate the license, which could result in us being unable to develop, manufacture and sell products that are covered by the licensed technology or enable a competitor to gain access to the licensed technology. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

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

In addition to seeking patent protection for certain aspects of our product candidates and delivery technologies, we also consider trade secrets, including confidential and unpatented know-how, important to the maintenance of our competitive position. We protect trade secrets and confidential and unpatented know-how, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to such knowledge, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants that obligate them to maintain confidentiality and assign their inventions to us. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts in the U.S. and certain foreign jurisdictions are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

We are also subject both in the U.S. and outside the U.S. to various regulatory schemes regarding requests for the information we provide to regulatory authorities, which may include, in whole or in part, trade secrets or confidential commercial information. While we are likely to be notified in advance of any disclosure of such information and would likely object to such disclosure, there can be no assurance that our challenge to the request would be successful.

We are currently, and may be in the future, subject to claims that we or our employees or consultants have wrongfully used or disclosed alleged trade secrets of our employees' or consultants' former employers or their clients. These claims may be costly to defend and if we do not successfully do so, we may be required to pay monetary damages, may be prohibited from using some of our research and development work, and may lose valuable intellectual property rights or personnel.

Many of our employees were previously employed at universities or biotechnology or pharmaceutical companies, including our competitors or potential competitors. From time to time, we have received correspondence from other companies alleging the improper use or disclosure, or inquiring regarding the use or disclosure, by certain of our employees who have previously been employed elsewhere in our industry, including with our competitors, of their former employer's trade secrets or other proprietary information.

Responding to these allegations can be costly and disruptive to our business, even when the allegations are without merit, and can be a distraction to management. On June 10, 2015, Alnylam filed a complaint against us in the Superior Court of Middlesex County, Massachusetts, alleging misappropriation of confidential information and trade secrets, as well as other related claims, in connection with our hiring of a number of former employees of Sirna, which at the time was a subsidiary of Merck, and in connection with our discussion with Merck to acquire Sirna, which was subsequently acquired by Alnylam. We may be subject to additional claims in the future that these or other employees of the Company have, or we have, inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending current or future claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, personnel, or the ability to use some of our research and development work. A loss of intellectual property, key research personnel, or their work product could hamper our ability to commercialize, or prevent us from commercializing, our product candidates, which could severely harm our business.

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

Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. Any trademark litigation could be expensive. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential collaborators or customers in our markets of interest. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

Risks Related to Government Regulation

We may be unable to obtain U.S. or foreign regulatory approval and, as a result, may be unable to commercialize our product candidates.

Our product candidates are subject to extensive governmental regulations relating to, among other things, research, development, testing, manufacture, quality control, approval, labeling, packaging, promotion, storage, record-keeping, advertising, distribution, sampling, pricing, sales and marketing, safety, post-approval monitoring and reporting, and export and import of drugs. Rigorous preclinical testing and clinical trials and an extensive regulatory approval process are required to be successfully completed in the U.S. and in many foreign jurisdictions before a new drug can be marketed. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. It is possible that none of the product candidates we may develop will obtain the regulatory approvals necessary for us or our collaborators to begin selling them.

We have very limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA as well as foreign regulatory authorities, such as the EMA. The time required to obtain FDA and foreign regulatory approvals is unpredictable but typically takes many years following the commencement of clinical trials, depending upon the type, complexity and novelty of the product candidate. The standards that the FDA and its foreign counterparts use when regulating us are not always applied predictably or uniformly and can change. Any analysis we perform of data from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also encounter unexpected delays or increased costs due to new government regulations, for example, from future legislation or administrative action, or from changes in the policy of the FDA or foreign regulatory authorities during the period of product development, clinical trials and regulatory review by the FDA or foreign regulatory authorities. It is impossible to predict whether legislative changes will be enacted, or whether FDA or foreign laws, regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be.

Because the drugs we are developing may represent a new class of drug, the FDA and its foreign counterparts have not yet established any definitive policies, practices or guidelines in relation to these drugs. While we believe the product candidates that we are currently developing are regulated as new drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA"), the FDA could decide to reclassify them, namely to regulate them or other products we may develop as biologics under the Public Health Service Act. The lack of policies, practices or guidelines may hinder or slow review by the FDA or foreign regulatory authorities of any regulatory filings that we may submit. Moreover, the FDA or foreign regulatory authorities may respond to these submissions by defining requirements we may not have anticipated. Such responses could lead to significant delays in the clinical development of our product candidates. In addition, because there may be approved treatments for some of the diseases for which we may seek approval, in order to receive regulatory approval, we may need to demonstrate through clinical trials that the product candidates we develop to treat these diseases, if any, are not only safe and effective, but safer or more effective than existing products.

Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenues from the particular product candidate for which we are seeking approval. Furthermore, any regulatory approval to market a product may be subject to limitations on the approved uses for which we may market the product or the labeling or other restrictions. Regulatory authorities also may impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. In addition, the FDA has the authority to require a REMS plan as part of an NDA or biologics license application or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug or biologic, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry. These limitations and restrictions may limit the size of the market for the product and affect coverage and reimbursement by third-party payors.

We are also subject to numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process varies among countries and may include all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval. Approval by the FDA does not ensure approval by regulatory authorities outside the U.S. and vice versa.

If we or our existing or future collaborators, manufacturers or service providers fail to comply with healthcare laws and regulations, we or they could be subject to enforcement actions, which could affect our ability to develop, market and sell our products and may harm our reputation.

We and our collaborators are or may become subject to federal, state, and foreign healthcare laws and regulations pertaining to fraud and abuse and patients' rights. These laws and regulations include, but are not limited to:

- the U.S. federal anti-kickback statute, which prohibits, among other things, persons from soliciting, receiving, offering or providing remuneration, directly or indirectly, to induce either the referral of an individual for a healthcare item or service, or the purchasing or ordering of an item or service, for which payment may be made under a federal healthcare program such as Medicare or Medicaid;
- the U.S. federal false claims act, which prohibits, among other things, individuals or entities from knowingly presenting or causing to be presented, claims for payment by government funded programs such as Medicare or Medicaid that are false or fraudulent, and which may apply to us by virtue of statements and representations made to customers or third parties;
- the FDCA and other laws, which prohibit promotion of drugs prior to FDA approval and prohibit dissemination of information about unapproved uses of approved drugs, with very specific and limited exceptions;
- HIPAA and HITECH, which prohibit executing a scheme to defraud healthcare programs, impose requirements relating to the privacy, security, and transmission of individually identifiable health information, and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information;
- the federal Physician Payment Sunshine Act ("Open Payments") requires that, among others, manufacturers of pharmaceutical and biological drugs covered by Medicare, Medicaid, and Children's Health Insurance Programs report certain payments and other transfers of value to U.S.-licensed physicians and teaching hospitals unless an exception applies; and
- state and foreign laws comparable to each of the above federal laws, such as, for example, state anti-kickback and false claims laws applicable to commercial insurers and other non-federal payors, requirements for mandatory corporate regulatory compliance or transparency reporting programs, and laws relating to patient data privacy and security.

If our operations are found to be in violation of any such requirements, we may be subject to penalties, including civil or criminal penalties, monetary damages, the curtailment or restructuring of our operations, loss of eligibility to obtain approvals from the FDA, or exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, any of which could adversely affect our financial results. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. Achieving and sustaining compliance with applicable laws and regulations may also be costly to us in terms of money, time and resources. In addition, many of the laws with which we must comply contain provisions added or amended by the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010, collectively referred to as the "ACA". The current Administration and the U.S. Congress have expressed a desire to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA, which has contributed to the uncertainty of the ongoing implementation and impact of the ACA and also underscores the potential for additional health care reform going forward.

If we or our collaborators, manufacturers or service providers fail to comply with applicable federal, state or foreign healthcare laws or regulations, we could be subject to enforcement actions, which could affect our ability to develop, market and sell our products successfully and could harm our reputation and lead to reduced acceptance of our products by the market. These enforcement actions include, among others:

- adverse regulatory inspection findings;
- warning or untitled letters;
- voluntary or mandatory product recalls or public notification or medical product safety alerts to healthcare professionals;

- restrictions on, or prohibitions against, marketing our products;
- restrictions on, or prohibitions against, importation or exportation of our products;
- suspension of review or refusal to approve pending applications or supplements to approved applications;
- limitations on our ability to secure or maintain adequate coverage and reimbursement for our proprietary product candidates from government (including U.S. federal health care programs) and private payors;
- exclusion from participation in government-funded healthcare programs (including Medicare and Medicaid);
- exclusion from eligibility for the award of government contracts for our products;
- FDA debarment of individuals at our Company;
- suspension or withdrawal of product approvals;
- seizure or administrative detention of products;
- injunctions; and
- civil and criminal penalties and fines.

Any drugs we develop may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, thereby harming our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drugs vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. Although we intend to monitor these regulations, our programs are currently in the early stages of development and we will not be able to assess the impact of price regulations for a number of years. As a result, we might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product and negatively impact the revenues we are able to generate from the sale of the product in that country.

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. However, there may be significant delays in obtaining coverage for newly-approved drugs. Moreover, eligibility for coverage does not necessarily signify that a drug will be reimbursed in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution costs. Also, interim payments for new drugs, if applicable, may be insufficient to cover our costs and may not be made permanent. Thus, even if we succeed in bringing one or more products to the market, these products may not be considered cost-effective, and the amount reimbursed for any products may be insufficient to allow us to sell our products on a competitive basis. Because our programs are in the early stages of development, we are unable at this time to determine their cost effectiveness, their coverage prospects, or the likely level or method of reimbursement, if covered. Increasingly, the third-party payors who reimburse patients or healthcare providers, such as government and private insurance plans, are seeking greater upfront discounts, additional rebates and other concessions to reduce the prices for pharmaceutical products. Moreover, legislation and regulations affecting the pricing of pharmaceuticals may change before regulatory agencies approve our proposed products for marketing and could further limit pricing approvals for, and reimbursement of, our products from government authorities and third-party payers. For example, the current Administration has indicated support for possible new measures related to drug pricing. New government legislation or regulations related to pricing or a government or third-party payer decision not to approve pricing for, or provide adequate coverage and reimbursements of, our products hold the potential to limit severely market acceptance of such products. If the price we are able to charge for any products we develop, or the reimbursement provided for such products, is inadequate in light of our development and other costs, our return on investment could be adversely affected.

We currently expect that certain drugs we develop may need to be administered under the supervision of a physician on an outpatient basis. Under currently applicable U.S. law, certain drugs that are not usually self-administered (including injectable drugs) may be eligible for coverage under the Medicare Part B program if certain requirements, including the following, have been satisfied:

- they are furnished incident to a physician's services;
- they are reasonable and necessary for the diagnosis or treatment of the illness or injury for which they are administered according to accepted standards of medical practice;
- they are included or approved for inclusion in certain Medicare-designated pharmaceutical compendia; and
- they have been approved by the FDA.

Under current law, as a condition of receiving Medicare Part B reimbursement (the Medicare program that generally covers physician-administered, outpatient drugs) for a manufacturer's eligible drugs or biologicals, the manufacturer is required to participate in other government healthcare programs, including the Medicaid Drug Rebate Program and the 340B Drug Pricing Program. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Under the 340B Drug Pricing Program, the manufacturer must extend discounts to entities eligible to participate in the program. Average prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S. Reimbursement rates under Medicare Part B would depend in part on whether the newly approved product would be eligible for a unique billing code. Self-administered, outpatient drugs are typically reimbursed by Medicare under Medicare Part D, and drugs that are administered in an inpatient hospital setting are typically reimbursed under Medicare Part A under a bundled payment. It is difficult for us to predict how Medicare coverage and reimbursement policies will be applied to our products in the future and coverage and reimbursement under different federal healthcare programs are not always consistent. Medicare reimbursement rates may also reflect budgetary constraints placed on the Medicare program.

Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for new drugs that we develop and for which we obtain regulatory approval could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our financial condition.

We believe that the efforts of governments and third-party payors to contain or reduce the cost of healthcare and legislative and regulatory proposals to broaden the availability of healthcare will continue to affect the business and financial condition of pharmaceutical and biopharmaceutical companies. A number of legislative and regulatory changes in the healthcare system in the U.S. and other major healthcare markets have been proposed, and such efforts have expanded substantially in recent years. These developments could, directly or indirectly, affect our ability to sell our products, if approved, at a favorable price.

For example, in the U.S., the ACA contains provisions that affect companies in the pharmaceutical industry and other healthcare-related industries in a variety of ways. Provisions that may affect pharmaceutical companies include, but are not limited to, the following:

- mandatory rebates for drugs sold under the Medicaid program have been increased, and the rebate requirement has been extended to drugs used in risk-based Medicaid managed care plans.
- the 340B Drug Pricing Program has been extended to require discounts for "covered outpatient drugs" sold to certain children's hospitals, critical access hospitals, freestanding cancer hospitals, rural referral centers, and sole community hospitals.
- pharmaceutical companies are required to offer discounts on brand-name drugs to patients who fall within the Medicare Part D coverage gap, commonly referred to as the "Donut Hole";
- pharmaceutical companies are required to pay an annual non-tax-deductible fee to the federal government based on each company's market share of prior year total sales of branded drugs to certain federal healthcare programs, such as Medicare, Medicaid, Department of Veterans Affairs and Department of Defense. Since we expect our branded pharmaceutical sales to constitute a small portion of the total federal healthcare program pharmaceutical market, we do not expect this annual assessment to have a material impact on our financial condition; and

- if the FDA were to reclassify any of our existing product candidates or choose to classify any of our future product candidates as biologics, then marketing approval for a follow-on biologic product may not become effective until 12 years after the date on which the reference innovator biologic product was first licensed by the FDA, with a possible six-month extension for pediatric products. After this exclusivity ends, the FDA may approve a biosimilar product to enter the market, which is likely to reduce the pricing for the innovator product and could affect our profitability if our products are classified as biologics.

In addition, in recent years, the U.S. Congress has enacted various laws seeking to reduce the federal debt level and contain healthcare expenditures. For example, the Budget Control Act of 2011 ("BCA") called for the establishment of a Joint Select Committee on Deficit Reduction, tasked with reducing the federal debt level. However, because the Committee did not draft a proposal by the BCA's deadline, President Obama issued a sequestration order on March 1, 2013 that imposed automatic spending cuts on various federal programs. Under the Bipartisan Budget Act of 2013 and a bill signed by the President on February 15, 2014, sequestration has been extended through fiscal year 2024. Medicare payments to providers are subject to such cuts, although the BCA generally limited the Medicare cuts to two percent. For fiscal year 2024, however, Medicare sequestration amounts will be realigned such that there will be a 4.0 percent sequester for the first six months and a zero percent sequester for the second six months.

The financial impact of the U.S. healthcare reform legislation over the next few years will depend on a number of factors, including the policies reflected in implementing regulations and guidance and changes in sales volumes for products affected by the legislation. Moreover, we cannot predict what healthcare reform initiatives may be adopted in the future. For example, the current Administration and the U.S. Congress have expressed a desire to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA, which has contributed to the uncertainty of the ongoing implementation and impact of the ACA and also underscores the potential for additional health care reform going forward. There is still uncertainty with respect to the impact the current Administration and the U.S. Congress may have, if any, and any changes will likely take time to unfold. We cannot assure you that the ACA, as currently enacted or as amended in the future, will not adversely affect our business and financial results. Moreover, further federal and state legislative, regulatory, or judicial developments are likely, and we expect ongoing initiatives in the U.S. to reduce healthcare expenditures. Such reforms could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

The healthcare industry is heavily regulated in the U.S. at the federal, state, and local levels, and our failure to comply with applicable requirements may subject us to penalties and negatively affect our financial condition.

As a healthcare company, our operations, clinical trial activities and interactions with healthcare providers may be subject to extensive regulation in the U.S., particularly if the Company receives FDA approval for any of its products in the future. For example, if we receive FDA approval for a product for which reimbursement is available under a federal healthcare program (e.g., Medicare, Medicaid), it would be subject to a variety of federal laws and regulations, including those that prohibit the filing of false or improper claims for payment by federal healthcare programs (e.g. the federal false claims act), prohibit unlawful inducements for the referral of business reimbursable by federal healthcare programs (e.g. the federal anti-kickback statute), and require disclosure of certain payments or other transfers of value made to U.S.-licensed physicians and teaching hospitals (Open Payments). We are not able to predict how third parties will interpret these laws and apply applicable governmental guidance and may challenge our practices and activities under one or more of these laws. If our past or present operations are found to be in violation of any of these laws, we could be subject to civil and criminal penalties, which could hurt our business, our operations and financial condition.

Similarly, HIPAA prohibits, among other offenses, knowingly and willfully executing a scheme to defraud any health care benefit program, including private payors, or falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for items or services under a health care benefit program. To the extent that the Company acts as a business associate to a healthcare provider that engages in electronic transactions, the Company may also be subject to the privacy and security provisions of HIPAA, as amended by HITECH, which restricts the use and disclosure of patient-identifiable health information, mandates the adoption of standards relating to the privacy and security of patient-identifiable health information, and requires the reporting of certain security breaches to healthcare provider customers with respect to such information. Additionally, many states have enacted similar laws that may impose more stringent requirements on entities like ours. Failure to comply with applicable laws and regulations could result in substantial penalties and adversely affect the Company's financial condition and results of operations.

Our ability to obtain services, reimbursement or funding from the federal government may be impacted by possible reductions in federal spending.

The U.S. federal budget remains in flux, which could, among other things, cut Medicare payments to providers. The Medicare program is frequently mentioned as a target for spending cuts. The full impact on our business of any future cuts in Medicare or other programs is uncertain. In addition, we cannot predict any impact that the current Administration may have on the federal budget. If federal spending is reduced, anticipated budgetary shortfalls may also impact the ability of relevant agencies, such as the FDA or the NIH, to continue to function at current levels. Amounts allocated to federal grants and contracts may be reduced or eliminated. These reductions may also impact the ability of relevant agencies to timely review and approve drug research and development, manufacturing, and marketing activities, which may delay our ability to develop, market and sell any products we may develop.

If any of our product candidates receive marketing approval and we or others later identify undesirable side effects caused by the product candidate, our ability to market and derive revenue from the product candidates could be compromised.

In the event that any of our product candidates receive regulatory approval and we or others identify undesirable side effects, adverse events or other problems caused by one of our products, any of the following adverse events could occur, which could result in the loss of significant revenue to us and materially and adversely affect our results of operations and business:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we may need to recall the product or change the way the product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof;
- we may not be able to secure or maintain adequate coverage and reimbursement for our proprietary product candidates from government (including U.S. federal health care programs) and private payors;
- we may be subject to fines, restitution or disgorgement of profits or revenues, injunctions, or the imposition of civil penalties or criminal prosecution;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- regulatory authorities may require us to implement a REMS, or to conduct post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product; we may be required to create a Medication Guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Risks Related to Our Common Stock

We are an “emerging growth company” and a “smaller reporting company,” and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies will make our common stock less attractive to investors.

We are an “emerging growth company” as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including (1) not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act of 2002 (Sarbanes-Oxley Act), (2) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and (3) 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 could be an emerging growth company for up to five years, although circumstances could cause us to lose that status earlier, including if the market value of our common stock held by non-affiliates exceeds $700.0 million as of the prior June 30 or if we have total annual gross revenue of $1.0 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31, or if we issue more than $1.0 billion in non-convertible debt during any three-year period before that time, in which case we would no longer be an emerging growth company immediately. Even after we no longer qualify as an emerging growth company, we may, under certain circumstances, still qualify as a “smaller reporting company” which would allow us to take advantage of many of the same exemptions from disclosure requirements including not being required to comply with

the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may 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 share price may be more volatile.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Our stock price is volatile and purchasers of our common stock could incur substantial losses.

Our stock price is volatile. From January 30, 2014, the first day of trading of our common stock, through November 1, 2017, the closing sale price of our common stock has ranged between a high of $46.00 per share and a low of $2.45 per share. The market price for our common stock may be influenced by many factors, including the other risks described in this "Risk Factors" section and the following:

- the success or failure of competitive products or technologies;
- results of preclinical studies and clinical trials of our product candidates, or those of our competitors, our existing collaborator or any future collaborators;
- regulatory or legal developments in the U.S. and other countries, especially changes in laws or regulations applicable to our product candidates;
- introductions and announcements of new products by us, our commercialization collaborators, or our competitors, and the timing of these introductions or announcements;
- actions taken by regulatory agencies with respect to our or our competitors' product candidates, products, clinical studies, manufacturing process or sales and marketing terms;
- actual or anticipated variations in our financial results or those of companies that are perceived to be similar to us;
- the success of our or our competitors' efforts to acquire or in-license additional technologies, products or product candidates;
- developments concerning our or our competitors' collaborations, including but not limited to those with sources of manufacturing supply and commercialization partners;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures or capital commitments;
- our ability or inability to raise additional capital and the terms on which we raise it;
- the recruitment or departure of key personnel;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- actual or anticipated changes in earnings estimates or changes in stock market analyst recommendations regarding our common stock, other comparable companies or our industry generally;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- announcement and expectation of additional financing efforts;
- speculation in the press or investment community;
- trading volume of our common stock;

- sales of our common stock by us or our stockholders;
- the absence of lock-up agreements with the holders of substantially all of our outstanding shares in connection with the follow-on public offering of our common stock;
- the concentrated ownership of our common stock;
- changes in accounting principles;
- terrorist acts, acts of war or periods of widespread civil unrest;
- natural disasters and other calamities;
- general economic, industry and market conditions; and
- developments concerning complaints or litigation against us.

In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that has often been unrelated to the operating performance of the issuer. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance.

The future issuance of equity or of debt securities that are convertible into equity will dilute our share capital.

We may choose to raise additional capital in the future, depending on market conditions, strategic considerations and operational requirements. To the extent that additional capital is raised through the issuance of shares or other securities convertible into shares, our stockholders will be diluted. Future issuances of our common stock or other equity securities, or the perception that such sales may occur, could adversely affect the trading price of our common stock and impair our ability to raise capital through future offerings of shares or equity securities. We cannot predict the effect, if any, that future sales of common stock or the availability of common stock for future sales will have on the trading price of our common stock.

The employment agreements with our executive officers may require us to pay severance benefits to officers who are terminated in connection with a change of control of the Company, which could harm our financial condition.

Our executive officers are parties to employment agreements providing, in the event of a termination of employment in connection with a change of control of the Company, for significant cash payments for severance and other benefits and acceleration of vesting of up to all outstanding stock options. The accelerated vesting of options could result in dilution to our existing stockholders and reduce the market price of our common stock. The payment of these severance benefits could harm our financial condition. In addition, these potential severance payments may discourage or prevent third parties from seeking a business combination with us.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our target studies and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

As of September 30, 2017, our executive officers and directors, together with holders of five percent or more of our outstanding common stock and their respective affiliates, beneficially owned, in the aggregate, approximately 75% of our outstanding common stock, assuming conversion of all Redeemable Convertible Preferred, after application of the Conversion Blockers, and subject to outstanding options and warrants that are exercisable within 60 days after such date, based on the Forms 3 and 4 and Schedules 13D and 13G filed by them with the SEC. As a result, these stockholders, if acting together, will continue to have significant influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets and any other significant corporate transaction. The interests of these stockholders may not be the same as, or may even conflict with the interests of our other stockholders. For example, these stockholders could delay or prevent a change

of control of our Company, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our Company or our assets and might affect the prevailing market price of our common stock. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

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

Provisions in our amended and restated certificate of incorporation and our amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Because our board of directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt by our stockholders to replace current members of our management team. These provisions include:

- a prohibition on actions by our stockholders by written consent;
- a requirement that special meetings of stockholders, which the Company is not obligated to call more than once per calendar year, be called only by the chairman of our board of directors, our chief executive officer, our board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors, or, subject to certain conditions, by our secretary at the request of the stockholders holding of record, in the aggregate, shares entitled to cast not less than ten percent of the votes at a meeting of the stockholders (assuming all shares entitled to vote at such meeting were present and voted);
- advance notice requirements for election to our board of directors and for proposing matters that can be acted upon at stockholder meetings; and
- the authority of the board of directors to issue preferred stock, such as the Redeemable Convertible Preferred, with such terms as the board of directors may determine.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, as amended, which prohibits a person who owns in excess of 15 percent of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15 percent of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. These provisions would apply even if the proposed merger or acquisition could be considered beneficial by some stockholders.

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

As a public company, we incur, and particularly after we are no longer an emerging growth company and if we ever cease to be a smaller reporting company, we will incur significant legal, accounting and other expenses that we did not incur as a private company.

The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the NASDAQ and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly. For example, we expect that these rules and regulations make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors. However, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

We are not currently required to comply with the rules of the SEC that implement Section 404(b) of the Sarbanes-Oxley Act. Pursuant to Section 404 of the Sarbanes-Oxley Act ("Section 404"), we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company and a smaller reporting company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. In addition, if we are not able to continue to meet these requirements, we may not be able to remain listed on The NASDAQ Global Select Market.

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

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

We may incur significant costs from class action litigation due to our historical or expected stock volatility.

Our stock price has fluctuated and may fluctuate for many reasons, including as a result of public announcements regarding the progress of our development efforts or the development efforts of our collaborators or competitors, the addition or departure of our key personnel, variations in our quarterly operating results and changes in market valuations of pharmaceutical and biotechnology companies. This risk is especially relevant to us because pharmaceutical and biotechnology companies have experienced significant stock price volatility in recent years. When the market price of a stock has been volatile as our stock price has been and may be, holders of that stock have occasionally brought securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit of this type against us, even if the lawsuit is without merit, we could incur substantial costs defending the lawsuit. The lawsuit could also divert the time and attention of our management.

Our amended and restated bylaws designates the Court of Chancery of the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated bylaws provide that, subject to limited exceptions, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any 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, any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, as amended, our amended and restated certificate of incorporation or our amended and restated bylaws, any action to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws, any action to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws or any 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 amended and restated certificate of incorporation 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.

Our stockholders may experience significant dilution as a result of the conversion of our Redeemable Convertible Preferred, future equity offerings and exercise of outstanding options.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock. We cannot assure you that we will be able to sell shares or other securities in any offering at a price per share that is equal to or greater than the price paid by our existing shareholders, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share paid by our existing stockholders.

In addition, we have a significant number of securities convertible into, or allowing the purchase of, our common stock. On April 11, 2017, we issued 700,000 shares of Redeemable Convertible Preferred that are convertible at any time into shares of our common stock at the Conversion Price, and through September 30, 2017, we have issued an additional 40,126 shares of Redeemable Convertible Preferred as dividends paid in kind. As of November 1, 2017, we also had 544,577 shares of common stock reserved for future issuance under our stock incentive plans. As of that date, there were also stock options and awards to purchase 6,145,417 shares of our common stock outstanding and warrants to purchase 87,901 shares of our common stock outstanding. The exercise or conversion of outstanding options, warrants or other securities having an exercise price per share or conversion price that is less than the offering price per share paid by our existing stockholders will increase dilution to such stockholders.

Future sales of our common stock in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. As of November 1, 2017, we had 20,848,503 shares of common stock outstanding, all of which shares, other than shares held by our directors and certain officers, were eligible for sale in the public market, subject in some cases to compliance with the requirements of Rule 144, including the volume limitations and manner of sale requirements. In addition, shares of common stock issuable upon exercise of outstanding options and shares reserved for future issuances under our stock incentive plans will become eligible for sale in the public market to the extent permitted by applicable vesting requirements and subject in some cases to compliance with the requirements of Rule 144.

Risks Related to Our Private Placement and Redeemable Convertible Preferred

The issuance of shares of our Redeemable Convertible Preferred reduces the relative voting power of holders of our common stock and dilutes the ownership of such holders, and the conversion of our Redeemable Convertible Preferred may adversely affect the market price of our common stock.

Holders of our Redeemable Convertible Preferred are entitled to vote, on an as-converted basis, together with holders of our common stock on all matters submitted to a vote of the holders of our common stock. As a result, the issuance of the Redeemable Convertible Preferred effectively reduces the relative voting power of the holders of our common stock. Moreover, the conversion of the Redeemable Convertible Preferred to common stock would dilute the ownership interest of existing holders of our common stock, and any sales in the public market pursuant to the registration rights granted to the holders of the Redeemable Convertible Preferred of the common stock issuable upon conversion of the Redeemable Convertible Preferred could adversely affect prevailing market prices of our common stock. Sales by such holders of a substantial number of shares of our common stock in the public market, or the perception that such sales might occur, could have a material adverse effect on the price of our common stock.

The holders of shares of the Redeemable Convertible Preferred may exercise significant influence over us.

After application of the Conversion Blockers, holders of the Redeemable Convertible Preferred owned approximately 72% of our shares of common stock on an as-converted basis as of September 30, 2017. Holders of our Redeemable Convertible Preferred are entitled to vote, on an as-converted basis, together with holders of our common stock on all matters submitted to a vote of the holders of our common stock. As a result, the holders of shares of the Redeemable Convertible Preferred have the ability to significantly influence the outcome of any matter submitted for the vote of the holders of our common stock.

In addition, under the terms of the Certificate of Designation that governs the Redeemable Convertible Preferred, the Redeemable Convertible Preferred generally ranks, with respect to liquidation, dividends and redemption, senior to other securities and, so long as any shares of Redeemable Convertible Preferred remain outstanding, the approval of the holders of a majority of the Redeemable Convertible Preferred is required in order for the Company to, among other things, (i) amend, modify or fail to give effect to any right of holders of the Redeemable Convertible Preferred, (ii) change the authorized number of Redeemable Convertible Preferred or issue additional Redeemable Convertible Preferred or create a new class or series of equity securities or securities convertible into equity securities with equal or superior rights, preferences or privileges to those of the Redeemable Convertible Preferred in terms of liquidation preference, dividend rights or certain governance rights, (iii) issue shares of common stock or securities convertible into common stock while we have insufficient shares to effect the conversion of the Redeemable Convertible Preferred into common stock, (iv) declare or pay dividends or redeem or repurchase any capital stock (other than certain repurchases from employees, directors, advisors or consultants upon termination of service) or (v) incur certain indebtedness in excess of $10 million.

One of the holders of Redeemable Convertible Preferred was also granted a one-time right to nominate a director, Adam M. Koppel M.D., Ph.D. Dr. Koppel joins Brian K. Halak, Ph.D., Peter Kolchinsky, Ph.D., and Stephen J. Hoffman, M.D., Ph.D. on our board of directors as directors affiliated with or formerly affiliated with holders of Redeemable Convertible Preferred. Notwithstanding the fact that all directors are subject to fiduciary duties to us and to applicable law, the interests of these directors could potentially differ from the interests of our security holders as a whole or of our other directors.

The holders of Redeemable Convertible Preferred have rights, preferences and privileges that are not held by, and are preferential to, the rights of our common stockholders.

Upon our liquidation, dissolution or winding up, the holders of the Redeemable Convertible Preferred will be entitled to receive out of our assets, in preference to the holders of the common stock and any junior preferred stock, an amount per share equal to the greater of (i) the sum of the Accrued Value plus an amount equal to all accrued or declared and unpaid dividends on the Redeemable Convertible Preferred that have not previously been added to the Accrued Value, or (ii) the amount that such shares would have been entitled to receive if they had converted into common stock immediately prior to such liquidation, dissolution or winding up. In addition, upon consummation of a specified change of control transaction, each holder of Redeemable Convertible Preferred will be entitled to receive in preference to the holders of common stock and any junior preferred stock, an amount equal to the greater of (i) 101% of the sum of the Accrued Value plus an amount equal to all accrued or declared and unpaid dividends on the Redeemable Convertible Preferred that have not previously been added to the Accrued Value, or (ii) the amount that such shares would have been entitled to receive if they had converted into common stock immediately prior to such event. These provisions may make it more costly for a potential acquirer to engage in a business combination transaction with us. Provisions that have the effect of discouraging, delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock and could also affect the price that some investors are willing to pay for our common stock. If there are insufficient assets to pay in full such amounts, then the available assets will be ratably distributed to the holders of the Redeemable Convertible Preferred in accordance with the respective amounts that would be payable on such shares if all amounts payable thereon were paid in full. This will reduce the remaining amount of our assets, if any, available to distribute to holders of our common stock. The holders of Redeemable Convertible Preferred also have a preferential right to receive cumulative dividends on the Accrued Value of each share of Redeemable Convertible Preferred at an initial rate of 12% per annum, compounded quarterly, and subject to downward adjustment upon achievement of certain milestones, such as our entering into the BI Agreement, as discussed above. Dividends on the Redeemable Convertible Preferred are payable in kind and will accrue on the Accrued Value of each share of Redeemable Convertible Preferred until the earlier of conversion, redemption, consummation of a change of control, a liquidation event, or upon failure to mandatorily convert due to the Conversion Blockers or applicable regulatory restrictions.

In addition, the holders of Redeemable Convertible Preferred also have certain redemption and conversion rights, including the right to request redemption by the Company after the seventh anniversary of the closing of the Private Placement.

Our obligations to the holders of Redeemable Convertible Preferred could limit our ability to obtain additional financing or increase our borrowing costs, which could have an adverse effect on our financial condition. These preferential rights could also result in divergent interests between the holders of shares of Redeemable Convertible Preferred and holders of our common stock.

Sales of shares issued in recent placements may cause the market price of our shares to decline.

In connection with the Private Placement, we issued 700,000 shares of Redeemable Convertible Preferred, which are convertible at any time into shares of our common stock at an agreed conversion rate. We have agreed to grant the holders of Redeemable Convertible Preferred certain demand, shelf and "piggyback" registration rights with respect to the shares of common stock issuable upon conversion of the Redeemable Convertible Preferred. Upon the effectiveness of such registration statements, all shares of common stock issuable upon conversion of the Redeemable Convertible Preferred may be freely sold in the open market. The sale of a significant amount of these shares in the open market or the perception that these sales may occur could cause the market price of our common stock to decline or become highly volatile.

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

(a) Unregistered Sales of Equity Securities

On April 11, 2017, we issued and sold 700,000 shares of our newly designated Redeemable Convertible Preferred to the Investors at a purchase price of $100.00 per share, for total gross proceeds of $70.0 million, and through September 30, 2017, we have issued an additional 40,126 shares of Redeemable Convertible Preferred as payment in kind of cumulative dividends. The sale and issuance of shares of common stock upon exercise and conversion of the Redeemable Convertible Preferred were offered and sold by us pursuant to an exemption from the registration requirements of the Securities Act provided by Section 4(a)(2) thereunder. Each Investor represented that it was an "accredited investor" as defined in Regulation D promulgated under the Securities Act, that such securities were being acquired for its own account for investment and not with a view toward distribution in a manner which would violate the Securities Act and that they could bear the economic risks of the investment. Appropriate legends were affixed to the instruments representing the securities issued in such transaction. See Part II, Item 2 "Management's Discussion and Analysis of Financial Condition and Results of Operations—Redeemable Convertible Preferred Stock" for a more detailed discussion of the Private Placement.

(b) Use of Proceeds

Not applicable.

(c) Issuer Purchases of Equity Securities

We did not repurchase any of our equity securities during the period covered by this report.

Item 3. DEFAULTS UPON SENIOR SECURITIES

Not applicable.

Item 4. MINE SAFETY DISCLOSURES

Not applicable.

Item 5. OTHER INFORMATION

None.

Item 6. EXHIBITS

Exhibit Number	Description of Documents
31.1(1)	Certification of the Company's principal executive officer required by Rule 13a-14(a) or Rule 15d-14(a).
31.2(1)	Certification of the Company's principal financial officer required by Rule 13a-14(a) or Rule 15d-14(a).
32.1*	Section 1350 Certifications.
101(1)	The following materials from the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2017, formatted in XBRL (eXtensible Business Reporting Language), include: (i) the Condensed Consolidated Balance Sheets as of September 30, 2017 (unaudited) and December 31, 2016, (ii) the Condensed Consolidated Statements of Operations (unaudited) for the three and nine months ended September 30, 2017 and 2016, (iii) the Condensed Consolidated Statements of Cash Flows (unaudited) for the nine months ended September 30, 2017 and 2016, and (iv) the Notes to Condensed Consolidated Financial Statements (unaudited).

* Exhibit 32.1 is being furnished and shall not be deemed to be "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liability of that section, nor shall such exhibit be deemed to be incorporated by reference in any registration statement or other document filed under the Securities Act or the Exchange Act, except as otherwise stated in such filing.

(1) Filed herewith.

SIGNATURES

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

DICERNA PHARMACEUTICALS, INC.

Date: November 2, 2017

By: /s/ John B. Green, CPA

John B. Green, CPA
Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)

Exhibit 31.1

CERTIFICATIONS

I, Douglas M. Fambrough, III, Ph.D., certify that:

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

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

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

4. The registrant's other certifying officer(s) 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.

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

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

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

Date: November 2, 2017

/s/ Douglas M. Fambrough, III, Ph.D.

Douglas M. Fambrough, III, Ph.D.
President, Chief Executive Officer and Director

Exhibit 31.2

CERTIFICATIONS

I, John B. Green, CPA, certify that:

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

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

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

4. The registrant's other certifying officer(s) 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 my 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.

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

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

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

Date: November 2, 2017

/s/ John B. Green, CPA

John B. Green, CPA
Chief Financial Officer

Exhibit 32.1

SECTION 1350 CERTIFICATIONS*

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. § 1350), Douglas M. Fambrough, III, Ph.D., President, Chief Executive Officer and Director of Dicerna Pharmaceuticals, Inc. (the "Company"), and John B. Green, Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

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

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

Dated: November 2, 2017

/s/ Douglas M. Fambrough, III, Ph.D.	/s/ John B. Green, CPA
Douglas M. Fambrough, III, Ph.D.	**John B. Green, CPA**
President, Chief Executive Officer and Director	**Chief Financial Officer**

* This certification accompanies the Quarterly Report on Form 10-Q, to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing.