

Dicerna Pharmaceuticals Inc  
Form 10-Q  
November 07, 2016  
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**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**  
**Washington, DC 20549**

**Form 10-Q**

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

**For the quarterly period ended September 30, 2016**

**OR**

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

**For the transition period from \_\_\_\_\_ to \_\_\_\_\_**

**Commission File Number: 001-36281**

**DICERNA PHARMACEUTICALS, INC.**

**(Exact name of registrant as specified in its charter)**

|                                                                                                    |                                                                         |
|----------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|
| <b>Delaware</b><br><b>(State or other jurisdiction of</b><br><b>incorporation or organization)</b> | <b>20-5993609</b><br><b>(IRS Employer</b><br><b>Identification No.)</b> |
| <b>87 Cambridgepark Drive</b>                                                                      |                                                                         |
| <b>Cambridge, MA 02140</b>                                                                         |                                                                         |
| <b>(Address of principal executive offices and zip code)</b>                                       |                                                                         |
| <b>(617) 621-8097</b>                                                                              |                                                                         |
| <b>(Registrant's telephone number, including area code)</b>                                        |                                                                         |

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 ☐

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

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Large accelerated filer ☐ Accelerated filer ☐  
Non-accelerated filer ☒ (Do not check if a smaller reporting company) Smaller reporting company ☐  
Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

As of November 4, 2016, there were 20,753,001 shares of the registrant's common stock, par value \$0.0001 per share, outstanding.

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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, and Section 21E of the Securities Exchange Act of 1934, as amended. 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, potential, ongoing or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

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, 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 products 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 collaborator, 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 arrangement with any future collaborator;

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 I, 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

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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 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 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.

**Table of Contents****PART I. FINANCIAL INFORMATION****Item 1. Financial Statements****Dicerna Pharmaceuticals, Inc.****Condensed Consolidated Balance Sheets****(Unaudited)**

(In thousands, except share and per share data)

|                                                                                                                                               | <b>September 30,<br/>2016</b> | <b>December 31,<br/>2015</b> |
|-----------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|------------------------------|
| <b>ASSETS</b>                                                                                                                                 |                               |                              |
| <b>CURRENT ASSETS:</b>                                                                                                                        |                               |                              |
| Cash and cash equivalents                                                                                                                     | \$ 32,544                     | \$ 56,058                    |
| Held-to-maturity investments                                                                                                                  | 25,002                        | 38,551                       |
| Prepaid expenses and other current assets                                                                                                     | 1,836                         | 1,532                        |
| Total current assets                                                                                                                          | 59,382                        | 96,141                       |
| <b>NONCURRENT ASSETS:</b>                                                                                                                     |                               |                              |
| Property and equipment net                                                                                                                    | 2,373                         | 2,684                        |
| Assets held in restriction                                                                                                                    | 1,116                         | 1,116                        |
| Other noncurrent assets                                                                                                                       | 78                            | 82                           |
| Total noncurrent assets                                                                                                                       | 3,567                         | 3,882                        |
| <b>TOTAL ASSETS</b>                                                                                                                           | <b>\$ 62,949</b>              | <b>\$ 100,023</b>            |
| <b>LIABILITIES AND STOCKHOLDERS EQUITY</b>                                                                                                    |                               |                              |
| <b>CURRENT LIABILITIES:</b>                                                                                                                   |                               |                              |
| Accounts payable                                                                                                                              | \$ 3,657                      | \$ 2,621                     |
| Accrued expenses and other current liabilities                                                                                                | 6,160                         | 6,380                        |
| Total current liabilities                                                                                                                     | 9,817                         | 9,001                        |
| <b>TOTAL LIABILITIES</b>                                                                                                                      | <b>9,817</b>                  | <b>9,001</b>                 |
| <b>STOCKHOLDERS EQUITY:</b>                                                                                                                   |                               |                              |
| Preferred stock, \$0.0001 par value 5,000,000 shares authorized, no shares issued and outstanding at September 30, 2016 and December 31, 2015 |                               |                              |
| Common stock, \$0.0001 par value 150,000,000 shares authorized at September 30, 2016 and December 31, 2015; 20,753,001 and 20,594,575         | 2                             | 2                            |

shares issued and outstanding at September 30, 2016 and December 31, 2015,  
respectively

|                                                   |                  |                   |
|---------------------------------------------------|------------------|-------------------|
| Additional paid-in capital                        | 294,864          | 287,263           |
| Accumulated deficit                               | (241,734)        | (196,243)         |
| Total stockholders' equity                        | 53,132           | 91,022            |
| <b>TOTAL LIABILITIES AND STOCKHOLDERS' EQUITY</b> | <b>\$ 62,949</b> | <b>\$ 100,023</b> |

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

**Table of Contents****Dicerna Pharmaceuticals, Inc.****Condensed Consolidated Statements of Operations****(Unaudited)****(In thousands, except share and per share data)**

|                                                       | <b>Three Months Ended September 30,</b> |  | <b>2016</b> |    | <b>2015</b> |            | <b>Nine Months Ended September 30,</b> |  | <b>2016</b> |    | <b>2015</b> |            |
|-------------------------------------------------------|-----------------------------------------|--|-------------|----|-------------|------------|----------------------------------------|--|-------------|----|-------------|------------|
|                                                       |                                         |  |             |    |             |            |                                        |  |             |    |             |            |
| Revenues                                              | \$                                      |  | 162         | \$ |             |            | \$                                     |  | 162         | \$ |             | 184        |
| Operating expenses:                                   |                                         |  |             |    |             |            |                                        |  |             |    |             |            |
| Research and development                              |                                         |  | 10,061      |    |             | 12,142     |                                        |  | 32,357      |    |             | 32,708     |
| General and administrative                            |                                         |  | 4,338       |    |             | 4,857      |                                        |  | 13,478      |    |             | 14,822     |
| Total operating expenses                              |                                         |  | 14,399      |    |             | 16,999     |                                        |  | 45,835      |    |             | 47,530     |
| Loss from operations                                  |                                         |  | (14,237)    |    |             | (16,999)   |                                        |  | (45,673)    |    |             | (47,346)   |
| Interest income                                       |                                         |  | 61          |    |             | 55         |                                        |  | 182         |    |             | 142        |
| Net loss                                              | \$                                      |  | (14,176)    | \$ |             | (16,944)   | \$                                     |  | (45,491)    | \$ |             | (47,204)   |
| Net loss per share basic and diluted                  | \$                                      |  | (0.68)      | \$ |             | (0.82)     | \$                                     |  | (2.20)      | \$ |             | (2.47)     |
| Weighted average shares outstanding basic and diluted |                                         |  | 20,752,416  |    |             | 20,592,840 |                                        |  | 20,708,600  |    |             | 19,097,230 |

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

**Table of Contents****Dicerna Pharmaceuticals, Inc.****Condensed Consolidated Statements of Cash Flows****(Unaudited)****(In thousands, except share and per share data)**

|                                                                                       | <b>Nine Months Ended September 30,</b> |                 |
|---------------------------------------------------------------------------------------|----------------------------------------|-----------------|
|                                                                                       | <b>2016</b>                            | <b>2015</b>     |
| <b>CASH FLOWS FROM OPERATING ACTIVITIES:</b>                                          |                                        |                 |
| Net loss                                                                              | \$ (45,491)                            | \$ (47,204)     |
| Adjustments to reconcile net loss to net cash used in operating activities:           |                                        |                 |
| Depreciation and amortization                                                         | 627                                    | 529             |
| Net amortization of premium/discount on investments                                   | 65                                     | 100             |
| Stock-based compensation                                                              | 7,067                                  | 7,374           |
| Changes in operating assets and liabilities:                                          |                                        |                 |
| Prepaid expenses and other assets                                                     | (300)                                  | (459)           |
| Accounts payable                                                                      | 983                                    | 133             |
| Accrued expenses and other liabilities                                                | (108)                                  | 3,998           |
| <b>Net cash used in operating activities</b>                                          | <b>(37,157)</b>                        | <b>(35,529)</b> |
| <b>CASH FLOWS FROM INVESTING ACTIVITIES:</b>                                          |                                        |                 |
| Changes in assets held in restriction                                                 |                                        | 264             |
| Purchases of property and equipment                                                   | (375)                                  | (995)           |
| Maturities of held-to-maturity investments                                            | 33,500                                 | 53,500          |
| Purchases of held-to-maturity investments                                             | (20,016)                               | (36,130)        |
| <b>Net cash provided by investing activities</b>                                      | <b>13,109</b>                          | <b>16,639</b>   |
| <b>CASH FLOWS FROM FINANCING ACTIVITIES:</b>                                          |                                        |                 |
| Proceeds from stock option exercises and issuances under Employee Stock Purchase Plan | 561                                    | 403             |
| Settlement of restricted stock for tax withholding                                    | (27)                                   | (75)            |
| Proceeds from public offering of common stock, net of costs                           |                                        | 45,438          |
| <b>Net cash provided by financing activities</b>                                      | <b>534</b>                             | <b>45,766</b>   |
| <b>(DECREASE) INCREASE IN CASH AND CASH EQUIVALENTS</b>                               | <b>(23,514)</b>                        | <b>26,876</b>   |
| <b>CASH AND CASH EQUIVALENTS Beginning of period</b>                                  | <b>56,058</b>                          | <b>26,067</b>   |

|                           |               |    |        |    |        |
|---------------------------|---------------|----|--------|----|--------|
| CASH AND CASH EQUIVALENTS | End of period | \$ | 32,544 | \$ | 52,943 |
|---------------------------|---------------|----|--------|----|--------|

SUPPLEMENTAL CASH FLOW INFORMATION:

|                                                                                    |    |    |    |
|------------------------------------------------------------------------------------|----|----|----|
| Property and equipment purchases included in accounts payable and accrued expenses | \$ | 52 | \$ |
|------------------------------------------------------------------------------------|----|----|----|

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

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**DICERNA PHARMACEUTICALS, INC.**

**Notes to Condensed Consolidated Financial Statements**

**(Unaudited)**

(In thousands, except share and per share data)

**1. Description of Business and Basis of Presentation**

***Nature of business***

Dicerna Pharmaceuticals, Inc. and its subsidiaries (the Company) is a biopharmaceutical company focused on the discovery and development of innovative subcutaneously delivered RNA interference (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, cardiovascular diseases, and viral infectious diseases. All of the Company's 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 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 Company is using its proprietary GalXC RNAi platform to build a broad pipeline in these therapeutic areas. The Company intends to discover, develop and commercialize novel therapeutics either on its own or in collaboration with pharmaceutical partners.

The Company continues to be subject to a number of risks common to companies in similar stages of development. Principal among these risks are the uncertainties of technological innovations, which are particularly high in the field of drug discovery and development, dependence on key individuals, development of the same or similar technological innovations by the Company's competitors and protection of proprietary technology.

The Company's ability to fund its planned preclinical and clinical operations, including completion of its clinical trials, will depend on its ability to raise capital through a combination of public or private equity offerings, debt financings, and research collaborations and license agreements. If we are unable to generate funding from one or more of these sources within a reasonable timeframe, we may have to delay, reduce or terminate our research and development programs, pre-clinical or clinical trials or undergo reductions in our workforce or other corporate restructuring activities. Based on our current operating plan, 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 next 12 months. We cannot predict whether additional funding will be available to us on acceptable terms or at all.

In May 2015, the Company completed the sale of 2,750,000 shares of common stock in a public offering of its common stock at a price to the public of \$17.75 per share, resulting in proceeds to the Company of \$45.4 million after deducting underwriting discounts and commissions of approximately \$2.9 million and offering costs incurred by the

Company of approximately \$0.4 million.

In September 2016, the Company announced that it transitioned its development program for primary hyperoxaluria (PH) to its GalXC-based DCR-PHXC product candidate from DCR-PH1, a lipid nanoparticle (LNP) formulated RNAi compound. DCR-PH1 was being studied in two clinical trials; one in patients with PH type 1 (PH1) and another in normal healthy volunteers. As part of this transition, the clinical studies for DCR-PH1 are being discontinued. The Company also announced the discontinuation of development efforts on its proprietary product candidate DCR-MYC for the treatment of MYC-related cancers, which was being studied in two clinical trials; a Phase 1 trial in patients with advanced solid tumors and hematological malignancies, including an expansion cohort in patients with pancreatic neuroendocrine tumors; and a Phase 1b/2 trial in patients with advanced hepatocellular carcinoma. Both clinical studies for DCR-MYC are being discontinued.

Since our inception in October 2006, we have devoted substantial resources to the research and development of DsiRNA and GalXC molecules, drug delivery technologies and the protection and enhancement of our intellectual property estate. We have no products approved for sale and all of our revenue to date has been collaboration revenue or government grant revenue. To date, we have funded our operations primarily through public offerings of our common stock, private placements of preferred stock and convertible debt securities, from research funding, license fees, option exercise fees, preclinical payments under our research collaboration and license agreement with the global pharmaceutical company Kyowa Hakko Kirin Co., Ltd. (KHK) and from government grants. More particularly, since our inception and through September 30, 2016, we have raised an aggregate of \$266.9 million to fund our operations, of which approximately \$45.4 million was from the May 2015 follow-on offering of common stock, \$0.3 million was from a federal government grant from the National Institutes of Health (NIH) covering our work on cancer treatment research, \$92.7 million was from the initial public offering of our common stock, which closed on February 4, 2014, \$110.5 million was from the sale of preferred stock and convertible debt securities (including \$3.0 million from the 2013 bridge note financing), \$17.5 million was

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through our collaboration and license agreement with KHK and \$0.5 million was from a federal government grant for our Qualifying Therapeutic Discovery Project in November 2010. As of September 30, 2016, we had cash and cash equivalents and held-to-maturity investments of \$57.5 million and we also had \$1.1 million in assets held in restriction.

***Basis of presentation and consolidation***

The accompanying unaudited condensed consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the U.S. (GAAP) and in accordance with the rules and regulations of the Securities and Exchange Commission (SEC) for interim financial information. Accordingly, they do not include all of the information and notes required by GAAP for a complete set of financial statements. The unaudited condensed consolidated interim financial statements have been prepared on the same basis as the annual 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, 2016 and results of operations and cash flows for the interim periods ended September 30, 2016 and 2015. These unaudited condensed consolidated interim financial statements should be read in conjunction with the audited consolidated financial statements and notes thereto included in the Company's Annual Report on Form 10-K for the year ended December 31, 2015. The results of the three and nine months ended September 30, 2016 are not necessarily indicative of the results to be expected for the year ending December 31, 2016 or for any other interim period or for any other future year.

**Summary of Significant Accounting Policies** There have been no material changes to the significant accounting policies previously disclosed in the Company's Annual Report on Form 10-K.

***Revenue Recognition***

Grant revenue is recognized in the period in which the related grant research and activities are incurred, provided that the conditions under which the grant was provided have been met and the Company only has perfunctory obligations outstanding. Any amounts received in advance of revenue recognition are classified as deferred revenue in the consolidated balance sheets. Costs associated with grants are included in research and development expenses in the consolidated statements of operations.

***Recent Accounting Pronouncements***

***Stock Compensation***

In March 2016, the FASB issued ASU No. 2016-09, Compensation - Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting. The new standard 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 on the statement of cash flows. The new standard will be effective for us on January 1, 2017. We are currently evaluating the potential impact that this standard may have on our financial position, results of operations and statement of cash flows.

***Leases***

In February 2016, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) No. 2016-02, Leases (Topic 842). The ASU requires lessees to put most leases on their balance sheets as a liability for the obligation to make lease payments and as a right-of-use asset, but recognize expenses on the income statements in a manner similar to today's accounting. The guidance also eliminates the current real estate-specific provisions for all

entities. For calendar-year public entities, the guidance becomes effective in 2019 and interim periods within that year. Early adoption is permitted for all entities. The Company has not chosen early adoption for this ASU and is currently evaluating its effect on the Company's consolidated financial statements.

### ***Income Taxes***

In November 2015, the FASB issued ASU No. 2015-17, Income Taxes (Topic 740): Balance Sheet Classification of Deferred Taxes. ASU No. 2015-17 simplifies the presentation of deferred income taxes by eliminating the separate classification of deferred income tax assets and liabilities into current and noncurrent amounts in the consolidated balance sheet statement of financial position. The amendments in the update require that all deferred tax assets and liabilities be classified as noncurrent in the consolidated balance sheet. The amendments in this update are effective for annual periods beginning after December 15, 2017, and interim periods therein and may be applied either prospectively or retrospectively to all periods presented. Early adoption is permitted. The Company has early adopted this standard in the fourth quarter of 2015 on a prospective basis, and it did not have an effect on the Company's consolidated financial statements.

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***Going Concern***

In August 2014, the FASB issued ASU No. 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*. ASU No. 2014-15 provides guidelines for determining when and how to disclose going concern uncertainties in the financial statements. The new standard requires management to perform interim and annual assessments of an entity's ability to continue as a going concern within one year of the date the financial statements are issued. An entity must provide certain disclosures if conditions or events raise substantial doubt about the entity's ability to continue as a going concern. ASU 2014-15 is effective for the Company for annual periods ending after December 15, 2016, and interim periods thereafter, with early adoption permitted. The adoption of ASU 2014-15 is not expected to have a material impact on the Company's consolidated financial statements.

***Revenue Recognition***

In May 2014, the FASB issued ASU No. 2014-09, Revenue from Contracts with Customers (Topic 606). ASU No. 2014-09 amends the guidance for accounting for revenue from contracts with customers. This ASU supersedes the revenue recognition requirements in Accounting Standards Codification Topic 605, Revenue Recognition, and creates a new Topic 606, Revenue from Contracts with Customers. This guidance was originally pronounced to become effective for fiscal years beginning after December 15, 2016, with early adoption not permitted. On July 9, 2015, the FASB decided to defer the effective date of the ASU by one year. As a result, the Company will be required to apply the new revenue standard to annual reporting periods beginning after December 15, 2017, and would be permitted to adopt the ASU early, but not before the original public organization effective date (annual periods beginning after December 15, 2016). Two adoption methods are permitted: retrospectively to all prior reporting periods presented, with certain practical expedients permitted; or retrospectively with the cumulative effect of initially adopting the ASU recognized at the date of initial application. The Company has not yet determined which adoption method it will utilize or the effect, if any, the adoption of this guidance will have on its consolidated financial statements through December 31, 2015 as the Company has yet to record revenue from contracts with customers.

**Table of Contents****2. Revenue Recognition*****NIH Grants***

In April 2015, the National Cancer Institute (NCI), a division of the National Institutes of Health (NIH), awarded the Company a grant related to cancer treatment research. The project period for this grant covered a six month period which commenced in April 2015, with total funds available of approximately \$0.2 million. The payment of the NIH grant award was based upon subcontractor and internal costs incurred that are specifically covered by the grant, and where applicable, a facilities and administrative rate that provides funding for overhead expenses. In August 2016, the NCI awarded an additional \$2.0 million for a second phase of the grant covering the period September 1, 2016 to February 28, 2018. Of this amount, \$1.0 million is committed funding and the additional funding commitment is expected in the third quarter of 2017, subject to NCI approval and availability of funds. The Company recognized zero and \$0.2 million of revenue associated with the NIH grant awards for the three and nine month periods ended September 30, 2015, respectively, and \$0.1 million of revenue for the three and nine month periods ended September 30, 2016.

**3. Held-to-maturity investments**

The Company invests its excess cash balances in short-term fixed-income investments. The Company determines the appropriate classification of investments at the time of purchase and re-evaluates such designation as of each balance sheet date. Debt securities carried at amortized cost are classified as held-to-maturity when the Company has the positive intent and ability to hold the securities to maturity.

The following tables provide information relating to held-to-maturity investments:

|                                                | <b>Amortized<br/>Cost</b> | <b>Gross<br/>Unrealized<br/>Gains</b> | <b>Gross<br/>Unrealized<br/>Losses</b> | <b>Fair<br/>Value</b> |
|------------------------------------------------|---------------------------|---------------------------------------|----------------------------------------|-----------------------|
| At September 30, 2016:                         |                           |                                       |                                        |                       |
| <b>Held-to-maturity investments</b>            |                           |                                       |                                        |                       |
| U.S. Government treasury and agency securities | \$ 25,002                 | \$ 14                                 | \$                                     | \$ 25,016             |

|                                                | <b>Amortized<br/>Cost</b> | <b>Gross<br/>Unrealized<br/>Gains</b> | <b>Gross<br/>Unrealized<br/>Losses</b> | <b>Fair<br/>Value</b> |
|------------------------------------------------|---------------------------|---------------------------------------|----------------------------------------|-----------------------|
| At December 31, 2015:                          |                           |                                       |                                        |                       |
| <b>Held-to-maturity investments</b>            |                           |                                       |                                        |                       |
| U.S. Government treasury and agency securities | \$ 38,551                 | \$                                    | \$ (47)                                | \$ 38,504             |

The amortized cost and fair value of held-to-maturity investments by contractual maturities at September 30, 2016, are as follows (in thousands):

|  | <b>Held-to-Maturity<br/>Amortized<br/>Cost</b> | <b>Fair<br/>Value</b> |
|--|------------------------------------------------|-----------------------|
|--|------------------------------------------------|-----------------------|

|                              |           |           |
|------------------------------|-----------|-----------|
| Maturing in one year or less | \$ 25,002 | \$ 25,016 |
| Total                        | \$ 25,002 | \$ 25,016 |

**Table of Contents****4. Stock-Based Compensation*****Stock option grants to employees***

During the three and nine month periods ended September 30, 2016, the Company granted stock options to purchase 30,000 and 1,475,275 shares of common stock to employees with grant date fair values of \$0.1 million and \$6.9 million, respectively, compared to 195,700 and 1,045,626 shares of common stock with grant date fair values of \$1.0 million and \$10.3 million, for the comparable three and nine month periods in 2015. Employee stock-based compensation for the three and nine month periods ended September 30, 2016 were \$2.3 million and \$7.1 million as compared to \$2.4 million and \$7.2 million, respectively, for the comparable 2015 periods. The assumptions used to estimate the grant date fair value for 2016 and 2015 grants were as follows:

|                                 | <b>Three Months Ended<br/>September 30, 2016</b> | <b>Nine Months Ended<br/>September 30, 2016</b> |
|---------------------------------|--------------------------------------------------|-------------------------------------------------|
| 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%                                           |

|                                 | <b>Three Months Ended<br/>September 30, 2015</b> | <b>Nine Months Ended<br/>September 30, 2015</b> |
|---------------------------------|--------------------------------------------------|-------------------------------------------------|
| Stock price                     | \$8.21                                           | \$8.21 \$24.03                                  |
| Expected option term (in years) | 6.25                                             | 5.50 6.25                                       |
| Expected volatility             | 71%                                              | 67% 71%                                         |
| Risk-free interest rate         | 1.54%                                            | 1.51% 1.81%                                     |
| Expected dividend yield         | 0.00%                                            | 0.00%                                           |

**5. Fair Value Measurements**

Fair value is an exit price, representing the amount that would be received from the sale of an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. Valuation techniques used to measure fair value are performed in a manner to maximize the use of observable inputs and minimize the use of unobservable inputs. As a basis for considering such assumption the accounting literature establishes a three-tier value hierarchy which prioritizes the inputs used in measuring fair value as follows: (Level 1) observable inputs, such as quoted prices in active markets; (Level 2) inputs other than the quoted prices in active markets that are observable either directly or indirectly; and (Level 3) unobservable inputs for which there is little or no market data, which requires the Company to develop its own assumptions.

A summary of the Company's assets that are measured or disclosed at fair value as of September 30, 2016 and December 31, 2015 are presented below:

| <b>Description</b> | <b>At September 30,<br/>2016</b> | <b>Level 1</b> | <b>Level 2</b> | <b>Level 3</b> |
|--------------------|----------------------------------|----------------|----------------|----------------|
|--------------------|----------------------------------|----------------|----------------|----------------|

|                              |    |        |           |           |    |
|------------------------------|----|--------|-----------|-----------|----|
| Cash equivalents             |    |        |           |           |    |
| Money market fund            | \$ | 27,821 | \$ 27,821 | \$        | \$ |
| Held-to-maturity investments |    |        |           |           |    |
| U.S. treasury securities     |    | 25,015 |           | 25,015    |    |
| Assets held in restriction   |    |        |           |           |    |
| Money market fund            |    | 1,116  |           | 1,116     |    |
| Total                        | \$ | 53,952 | \$ 27,821 | \$ 26,131 | \$ |

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| Description                  | At December 31, |           |           |         |
|------------------------------|-----------------|-----------|-----------|---------|
|                              | 2015            | Level 1   | Level 2   | Level 3 |
| Cash equivalents             |                 |           |           |         |
| Money market fund            | \$ 45,557       | \$ 45,557 | \$        | \$      |
| Held-to-maturity investments |                 |           |           |         |
| U.S. treasury securities     | 38,504          |           | 38,504    |         |
| Assets held in restriction   |                 |           |           |         |
| Money market fund            | 1,116           |           | 1,116     |         |
| Total                        | \$ 85,177       | \$ 45,557 | \$ 39,620 | \$      |

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, 2016 and December 31, 2015, respectively.

The Company's assets held in restriction 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 and 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, 2016 and December 31, 2015, respectively.

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 observable inputs as of September 30, 2016 and December 31, 2015, respectively.

For the three and nine month periods ended September 30, 2016 and 2015 there were no transfers between Level 1 and Level 2.

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**6. Commitments and Contingencies**

***Facility lease***

On July 11, 2014, the Company executed a non-cancelable operating lease for office and laboratory space in Cambridge, Massachusetts. The lease agreement obligates the Company to minimum lease payments totaling \$9.6 million over the six-year lease term. The lease commenced on December 1, 2014. As part of the lease agreement, the Company established a \$1.1 million letter of credit, secured by a money market account which is included in assets held in restriction at September 30, 2016 and December 31, 2015. As of September 30, 2016, the remaining lease obligations were \$6.9 million, of which \$1.6 million is payable within the next year.

***City of Hope license agreement***

In September 2007, the Company entered into a license agreement with City of Hope, an independent academic research and medical center (the "Medical Center"). In consideration for the right to develop, manufacture, and commercialize products based on certain of the Medical Center's intellectual property, the Company paid a one-time, non-refundable license fee and issued shares of common stock as consideration for the license.

The Company is required to pay an annual license maintenance fee, reimburse the Medical Center for patent costs incurred, and pay an amount within the range of \$5.0 million to \$10.0 million upon the achievement of certain milestones, and royalties on future sales, if any. There were no sublicense and other fees accrued at September 30, 2016 and December 31, 2015. The license agreement will remain in effect until the expiration of the last patents or copyrights licensed under the agreement or until all obligations under the agreement with respect to payment of milestones have terminated or expired. The Company may terminate the license agreement at any time upon 90 days written notice to the Medical Center. The Company recorded research and development expense, related to the agreement with the Medical Center, of zero and \$0.1 million for the three and nine month periods ended September 30, 2016 and 2015, respectively.

***Plant Bioscience Limited license agreement***

In September 2013, the Company entered into a commercial license agreement with Plant Bioscience Limited (PBL), pursuant to which PBL has granted to the Company a license to certain of its U.S. patents and patent applications to research, discover, develop, manufacture, sell, import and export, products incorporating one or more short RNA molecules (SRMs).

The Company has paid PBL a one-time, non-refundable signature fee and will pay PBL a nomination fee for any additional SRMs nominated by the Company under the agreement. The Company is further obligated to pay PBL milestone payments upon achievement of certain clinical and regulatory milestones. During 2014, the Company paid \$0.1 million to PBL based on meeting a clinical milestone. In addition, PBL is entitled to receive royalties of any net sale revenue of any licensed product candidates sold by the Company. The Company did not record any research and development expense, related to this agreement, during the three and nine month periods ended September 30, 2016 and 2015, respectively.

***Arbutus Biopharma Corporation license agreement***

In November 2014, the Company signed a licensing and collaboration agreement with Arbutus Biopharma Corporation (Arbutus) to license Arbutus' LNP delivery technology for exclusive use in the Company's primary hyperoxaluria type 1 (PH1) development program. The Company will use Arbutus' LNP technology to

deliver DCR-PH1, for the treatment of PH1. As of September 30, 2016, the Company paid \$3.0 million in cumulative license fees. There were no license fees recorded in the three and nine month periods ended September 30, 2016 and 2015, respectively. Arbutus is entitled to receive additional payments of \$22.0 million in aggregate development milestones, plus a mid-single-digit royalty on future PH1 sales. This partnership also includes a supply agreement with Arbutus providing clinical drug supply and regulatory support.

***Carnegie Institution of Washington license agreement***

In January 2009, the Company entered into a license agreement with the Carnegie Institution of Washington (Carnegie), pursuant to which Carnegie has granted to us a worldwide, non-exclusive license under certain of its patents and patent applications relating to genetic inhibition by double-stranded RNA molecules for internal research, screening and development of product candidates for human and non-human diagnostic and therapeutic uses. We have paid Carnegie a one-time upfront fee and will in addition pay an

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annual license fee during the term of the agreement. We are further obligated to make two additional payments of \$0.1 million each upon achievement of the filing with the FDA of an NDA for a licensed product candidate and the first commercial sale of a licensed product candidate or licensed method. Carnegie is entitled to receive royalties on any net sale revenue from licensed product candidates sold by us, with the royalty rate to be further negotiated between Carnegie and us in good faith reflecting customary rates in the industry.

The agreement will terminate with respect to each licensed product candidate upon the last to expire of any valid claim within the licensed patent rights. Each party may terminate the agreement upon any uncured material breach by the other party. We may terminate the agreement at any time for any reason upon written notice to Carnegie. Any patents associated with this license will expire in 2018, removing any obligations. The Company recorded research and development expense, related to the agreement with Carnegie, of zero and \$0.03 million for the three and nine month periods ended September 30, 2016 and 2015, respectively.

**7. Litigation**

On June 10, 2015, Alnylam Pharmaceuticals, Inc. (Alnylam) filed a complaint against the Company in the Superior Court of Middlesex County, Massachusetts. 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 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 it 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 outstanding as of September 30, 2016 and December 31, 2015.

**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**

We are a biopharmaceutical company focused on the discovery and development of innovative subcutaneously delivered RNA interference (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, 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. Within our therapeutic areas, we seek to

focus our drug discovery and development efforts on target genes where the connection between that target gene and the disease is well understood and documented.

The GalXC RNAi platform supports the Company's long-term strategy to retain a full or substantial ownership stake and invest internally for diseases with focused patient populations, such as certain rare diseases, as we see such diseases as representing opportunities that carry high probabilities of success, have easily identifiable patient populations and a limited number of centers of excellence to facilitate reaching these patients, and have the potential for more rapid clinical development programs. For more complex diseases with multiple gene dysfunctions and larger patient populations, we plan to pursue partnerships that can provide the enhanced scale, resources and commercial infrastructure required to maximize these prospects.

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**Table of Contents****GalXC 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. In addition to DCR-PHXC, which is in preclinical development, the Company expects to launch two more GalXC programs in 2016: one will focus on cardiovascular disease by targeting the PCSK9 gene; the other will focus on an undisclosed rare disease. The Company has the capacity to launch up to three additional programs annually, with the intent to advance five programs into the clinic by the end of 2019. Our 2016 development programs are as follows:

**Primary Hyperoxaluria (PH).** We are developing DCR-PHXC for the treatment of PH. PH is a rare inborn error 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. DCR-PHXC is in preclinical development, and is advancing into IND-enabling studies. We plan to file an Investigational New Drug (IND) submission or Clinical Trial Application (CTA) for DCR-PHXC in late 2017 and commence human clinical trials shortly thereafter. In the third quarter of 2016, we announced that we transitioned our PH program to DCR-PHXC from DCR-PH1, a lipid nanoparticle (LNP) formulated RNAi compound. The LNP delivery system was obtained through a licensing agreement with Arbutus Biopharma Corporation (formerly known as Tekmira Pharmaceuticals Corporation). DCR-PH1 was being studied in two clinical trials, DCR-PH1-101 in patients with primary hyperoxaluria type 1 (PH1) and DCR-PH1-102 in normal healthy volunteers (NHVs). We presented initial data from the NHV study at the 17th Congress of the International Pediatric Nephrology Association (IPNA) in Iguacu, Brazil on September 22, 2016. We believe these data provide the proof of concept for the pharmacological activity of RNAi-based therapy in PH.

**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. PCSK9 is a validated target for hypercholesterolemia, and there are FDA-approved therapies targeting PCSK9 that are based on monoclonal antibody (MAb) technology. Based on preclinical studies, we believe that our GalXC RNAi platform can produce a PCSK9-targeted therapy with more attractive commercial properties than existing MAb therapies, based on comparatively smaller subcutaneous injection volumes and less frequent dosing, while providing equal or superior control of serum cholesterol.

**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.

**2017 development programs.** We are currently using our GalXC RNAi platform to evaluate a series of target genes in multiple disease states. In 2017, we expect to initiate programs targeting the hepatitis

B virus, as well as two additional programs from our core therapeutic areas.

In addition to our GalXC development programs, we have partnered our early generation, non-GalXC RNAi technology against two targets, the KRAS oncogene and an additional undisclosed gene, with the global pharmaceutical company Kyowa Hakko Kirin Co., Ltd. (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. We expect that our strategy to partner the development of product candidates will help us fund the costs of clinical development and enable us to diversify risk across a number of programs. KHK is responsible for all preclinical and clinical development activities, including the selection of patient population and disease indications for clinical trials.

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We have also developed a wholly-owned clinical candidate, DCR-BCAT, targeting the  $\beta$ -catenin oncogene for tumors believed to be driven by activating mutations in  $\beta$ -catenin or other tumor-driving genes in the Wnt signaling pathway. In multiple animal models including both colorectal carcinoma and hepatocellular carcinoma tumor models, DCR-BCAT has shown anti-tumor efficacy in tumors driven by  $\beta$ -catenin and/or Wnt signaling pathway mutations. DCR-BCAT is based on an extended version of our earlier generation Dicer Substrate RNAi technology and is delivered by an advanced version of our lipid 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.

In oncology, we directed our development efforts towards our proprietary product candidate DCR-MYC for the treatment of MYC-related cancers, which was being investigated in two clinical trials: a Phase 1 trial in patients with advanced solid tumors and hematological malignancies, including an expansion cohort in patients with pancreatic neuroendocrine tumors; and a Phase 1b/2 trial in patients with advanced hepatocellular carcinoma (HCC). MYC is an oncogene frequently amplified or overexpressed in a wide variety of tumor types. In September 2016, we announced our plan to discontinue the clinical development programs for DCR-MYC. While preliminary data from the DCR-MYC-101 trial provided evidence of clinical response and molecular knockdown of MYC in patients, the early efficacy results from DCR-MYC-101 and DCR-MYC-102 in HCC did not meet the Company's expectations to warrant further development. Data from these studies was presented at the Oligonucleotide Therapeutics Society Conference on September 28, 2016.

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Since our inception in October 2006, we have devoted substantial resources to the research and development of DsiRNA and GalXC molecules, drug delivery technologies and the protection and enhancement of our intellectual property estate. We have no products approved for sale and all of our revenue to date has been collaboration revenue or government grant revenue. To date, we have funded our operations primarily through public offerings of our common stock, private placements of preferred stock and convertible debt securities, from research funding, license fees, option exercise fees, preclinical payments under our research collaboration and license agreement with KHK and from government grants. More particularly, since our inception and through September 30, 2016, we have raised an aggregate of \$266.9 million to fund our operations, of which approximately \$45.4 million was from the May 2015 follow-on offering of common stock, \$0.3 million was from a federal government grant from the National Institutes of Health (NIH) covering our work on cancer treatment research, \$92.7 million was from the initial public offering of our common stock, which closed on February 4, 2014, \$110.5 million was from the sale of preferred stock and convertible debt securities (including \$3.0 million from the 2013 bridge note financing), \$17.5 million was through our collaboration and license agreement with KHK and \$0.5 million was from a federal government grant for our Qualifying Therapeutic Discovery Project in November 2010. As of September 30, 2016, we had cash and cash equivalents and held-to-maturity investments of \$57.5 million and we also had \$1.1 million in assets held in restriction.

On May 27, 2015, we completed a follow-on offering of our common stock, in which we issued and sold a total of 2,750,000 shares of common stock, at a public offering price of \$17.75 per share. We received net proceeds of approximately \$45.4 million after deducting underwriting commissions and discounts and offering expenses payable by us.

Since inception, we have incurred significant operating losses. Our net loss was \$45.5 million, and \$47.2 million for the nine months ended September 30, 2016 and 2015, respectively. Substantially all of our operating losses resulted from expenses incurred in connection with our research and clinical programs and from general and administrative costs associated with our operations. We recognized \$0.1 million of revenue in the three and nine months ended September 30, 2016 and zero and \$0.2 million of revenue in the comparable periods in 2015. Our cumulative revenues to date have been generated through our research collaboration and license agreement with KHK and government grants. We have not generated any commercial product revenue. As of September 30, 2016, we had an accumulated deficit of \$241.7 million. We expect to continue to incur significant and potentially increasing losses in the foreseeable future. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses may increase as we:

advance our product candidates into preclinical development;

conduct clinical trials of our current and other potential product candidates;

continue our research and development efforts, including to expand our pipeline and to enhance our technology platform;

increase research and development related activities for the discovery and development of additional product candidates;

manufacture clinical study materials and develop large-scale manufacturing capabilities;

seek regulatory approval for our product candidates that successfully complete clinical trials;

maintain, expand and protect our intellectual property portfolio;

add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts;

respond to and defend ourselves against complaints and potential litigation, including the Alnylam complaint of misappropriation of confidential information; and

operate as a public company.

We do not expect to generate substantial revenue from product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our product candidates, which is subject to significant uncertainty and which could take several years. If we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Until such time, if ever, that 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. Our failure to raise capital or enter into such other arrangements within 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, pre-clinical or clinical trials or undergo reductions in our workforce or other corporate restructuring activities.

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**Table of Contents*****Collaboration agreement***

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 in oncology. We have granted KHK an exclusive, worldwide, royalty-bearing and sub-licensable license to our DsiRNA molecules and drug delivery technologies and intellectual property for two programs, KRAS and a second undisclosed oncology target. Under the research collaboration and license agreement, KHK is responsible for activities to develop, manufacture and commercialize the selected DsiRNA-based compounds and pharmaceutical products containing such compounds. For the KRAS product candidate, we have an option to co-promote in the U.S. for an equal share of the profits from U.S. net sales. In addition, 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.

Since the initiation of the research collaboration and license agreement, of the various targets in the collaboration, two target programs, including the initial target KRAS, have been nominated by KHK for formal development studies. Both programs utilize our specific RNAi-inducing double-stranded DsiRNA molecules and a lipid nanoparticle drug delivery technology proprietary to KHK. As of September 30, 2016, we have received total payments to date of \$17.5 million from KHK under the research collaboration and license agreement.

***License agreements***

In September 2007, we entered into a license agreement with City of Hope (COH), an independent academic research and medical center, pursuant to which COH has granted to us an exclusive (subject to certain exceptions described below), royalty-bearing, worldwide license under certain patent rights in relation to DsiRNA, including the core DsiRNA patent (U.S. 8,084,599), to manufacture, use, offer for sale, sell and import products covered by the licensed patent rights for the prevention and treatment of any disease in humans. COH is restricted from granting any additional rights to develop, manufacture, use, offer to sell, sell or import products covered by the licensed patent rights for the prevention and treatment of any disease in humans. In addition, COH has granted to us an exclusive, royalty-bearing, worldwide license under the licensed patent rights providing certain rights for up to 20 licensed products selected by us for human diagnostic uses, provided that COH has not granted or is not negotiating a license of rights to diagnostic uses for such licensed products to a third party. The core DsiRNA patent (U.S. 8,084,599), titled "methods and compositions for the specific inhibition of gene expression by double-stranded RNA," describes RNA structures having a 25 to 30 nucleotides sense strand, a blunt end at the 3' end of the sense strand and a one to four nucleotides overhang at the 3' end of the antisense strand. The expiration date of this patent is July 17, 2027.

Pursuant to the terms of the agreement, we paid COH a one-time, non-refundable license fee and issued shares of our common stock to COH and a co-inventor of the core DsiRNA patent. COH is entitled to receive milestone payments in an aggregate amount within the range of \$5.0 million to \$10.0 million upon achievement of certain clinical and regulatory milestones. COH is further entitled to receive royalties at a low single-digit percentage of any net sale revenue of the licensed products sold by us and our sublicensees. If we sublicense the licensed patent rights to a third party, COH has the right to receive a double digit percentage of sublicense income, the percentage of which decreases after we have expended \$12.5 million in development and commercialization costs. We are also obligated to pay COH an annual license maintenance fee, which may be credited against any royalties due to COH in the same year, and reimburse COH for expenses associated with the prosecution and maintenance of the license patent rights. The license agreement will remain in effect until the expiration of the last to expire of the patents or copyrights licensed under the agreement. We have not included our obligations to make future milestone payments on our balance sheet because the achievement and timing of the related milestones is not probable and estimable.

In September 2013, we entered into a commercial license agreement with Plant Bioscience Limited (PBL), pursuant to which PBL has granted a license to us for certain of its U.S. patents and patent applications to research, discover, develop, manufacture, sell, import and export, products incorporating one or more short RNA molecules (SRMs).

We have paid PBL a one-time, non-refundable signature fee and will pay PBL a nomination fee for any additional SRMs nominated by us under the agreement. We are further obligated to pay PBL milestone payments upon achievement of certain clinical and regulatory milestones. In addition, PBL is entitled to receive royalties on any net sale revenue of any licensed product candidates sold by us. During 2014, the Company paid \$0.1 million to PBL upon the commencement of our MYC clinical trial.

In November 2014, we entered into a licensing and collaboration agreement with Arbutus to license Arbutus LNP delivery technology for exclusive use in our PH1 development program. We will use Arbutus LNP technology to deliver DCR-PH1, for the treatment of PH1. As of September 30, 2016, we had paid a total of \$3.0 million in license fees to Arbutus. Arbutus is entitled to receive additional payments of \$22.0 million in aggregate development milestones, plus a mid-single-digit royalty on future PH1 sales. This partnership also includes a supply agreement with Arbutus providing clinical drug supply and regulatory support.

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In January 2009, we entered into a license agreement with the Carnegie Institution of Washington (Carnegie), pursuant to which Carnegie has granted to us a worldwide, non-exclusive license under certain of its patents and patent applications relating to genetic inhibition by double-stranded RNA molecules for internal research, screening and development of product candidates for human and non-human diagnostic and therapeutic uses. We have paid Carnegie a one-time upfront fee and will in addition pay an annual license fee during the term of the agreement. We are further obligated to make two one-time additional payments in the aggregate amount of \$0.1 million upon achievement of the filing with the FDA of an NDA for a licensed product candidate and the first commercial sale of a licensed product candidate or licensed method. Carnegie is entitled to receive royalties on any net sale revenue from licensed product candidates sold by us, with the royalty rate to be further negotiated between Carnegie and us in good faith reflecting customary rates in the industry. The Company recorded research and development expense, related to the agreement with Carnegie, of zero and \$0.03 million for the three and nine month periods ended September 30, 2016 and 2015, respectively.

The agreement will terminate with respect to each licensed product candidate upon the last to expire of any valid claim within the licensed patent rights. Each party may terminate the agreement upon any uncured material breach by the other party. We may terminate the agreement at any time for any reason upon written notice to Carnegie. Any patents associated with this license will expire in 2018, removing any obligations.

In December 2014, we licensed all of our non-U.S. intellectual property rights to a non-U.S. wholly-owned subsidiary, and, in December 2015, we licensed our U.S. intellectual property rights to the same wholly-owned subsidiary.

## **Financial Operations Overview**

### ***Revenue***

Our revenue to date has been generated primarily through research funding, license fees, option exercise fees and preclinical development payments under our research collaboration and license agreement with KHK and government grants. We have not generated any commercial product revenue. For each product candidate under our research collaboration and license agreement with KHK, we are also entitled to receive clinical, regulatory and commercialization milestone payments of up to \$110.0 million and royalties on net sales of such product candidate. We did not receive any royalty payments during the three and nine month periods ended September 30, 2016 or 2015.

In April 2015, the National Cancer Institute (NCI), a division of the National Institutes of Health (NIH), awarded us a grant related to cancer treatment research. The project period for this grant covered a six month period which commenced in April 2015, with total funds available of approximately \$0.2 million. The payment of the NIH grant award was based upon subcontractor and internal costs incurred that are specifically covered by the grant, and where applicable, a facilities and administrative rate that provides funding for overhead expenses. In August 2016, the NCI awarded an additional \$2.0 million for a second phase of the grant covering the period September 1, 2016 to February 28, 2018. Of this amount, \$1.0 million is committed funding and the additional funding commitment is expected in the third quarter of 2017, subject to NCI approval and availability of funds. The Company recognized zero and \$0.2 million of revenue associated with the NIH grant awards for the three and nine month periods ended September 30, 2015, respectively, and \$0.1 million of revenue for the three and nine month periods ended September 30, 2016.

In the future, we may generate revenue from a combination of research and development payments, license fees and other upfront payments, milestone payments, product sales and royalties in connection with our collaboration with KHK or future collaborations and licenses. We expect that any revenue we generate will fluctuate in future periods as a result of the timing of our or a collaborator's achievement of preclinical, clinical, regulatory and commercialization

milestones, if at all, the timing and amount of any payments to us relating to such milestones and the extent to which any of our product candidates are approved and successfully commercialized by us or a collaborator. If we, KHK or any future collaborator fails to develop product candidates in a timely manner or obtain regulatory approval for them, our ability to generate future revenue, and our results of operations and financial position, would be materially adversely affected.

***Research and development expenses***

Research and development expenses consist of costs associated with our research activities, including discovery and development of our DsiRNA and GalXC molecules and drug delivery technologies, clinical and pre-clinical development activities and our research activities under our research collaboration and license agreement with KHK. Our research and development expenses include:

direct research and development expenses incurred under arrangements with third parties, such as contract research organizations, contract manufacturing organizations, and consultants;

platform-related lab expenses, including lab supplies, license fees, consultants and our scientific advisory board;

employee-related expenses, including salaries, benefits and stock-based compensation expense; and

facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation of leasehold improvements and equipment and laboratory and other supplies.

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We expense research and development costs as they are incurred. We account for nonrefundable advance payments for goods and services that will be used in future research and development activities as expenses when the service has been performed or when the goods have been received. A significant portion of our research and development costs are not tracked by project as they benefit multiple projects or our technology platform.

In the rare disease area, we are developing DCR-PHXC for the treatment of PH. PH is a rare inborn error 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. DCR-PHXC is in preclinical development, and is advancing into IND-enabling studies. We plan to file an Investigational New Drug (IND) submission or Clinical Trial Application (CTA) for DCR-PHXC in late 2017 and commence human clinical trials shortly thereafter.

In September 2016, we announced that we transitioned our PH program to DCR-PHXC from DCR-PH1, a lipid nanoparticle (LNP) formulated RNAi compound. DCR-PH1 was being studied in two clinical trials, DCR-PH1-101 in patients with primary hyperoxaluria type 1 (PH1) and DCR-PH1-102 in normal healthy volunteers (NHVs). Both studies are being discontinued.

In oncology, we directed our development efforts towards our proprietary product candidate DCR-MYC for the treatment of MYC-related cancers, which was being investigated in two clinical trials: a Phase 1 trial in patients with advanced solid tumors and hematological malignancies, including an expansion cohort in patients with pancreatic neuroendocrine tumors; and a Phase 1b/2 trial in patients with advanced hepatocellular carcinoma (HCC). MYC is an oncogene frequently amplified or overexpressed in a wide variety of tumor types. In September 2016, we announced its plan to discontinue the clinical development programs for DCR-MYC. While preliminary data from the DCR-MYC-101 trial provided evidence of clinical response and molecular knockdown of MYC in patients, the early efficacy results from DCR-MYC-101 and DCR-MYC-102 in HCC did not meet the Company's expectations to warrant further development. Data from these studies was presented at the Oligonucleotide Therapeutics Society Conference on September 28, 2016.

The process of conducting preclinical studies and clinical trials necessary to obtain regulatory approval is costly and time-consuming. We, KHK or any future collaborator may never succeed in obtaining marketing approval for any of our product candidates. The probability of success for each product candidate may be affected by numerous factors, including preclinical data, clinical data, competition, manufacturing capability and commercial viability. All of our research and development programs are at an early stage and successful development of future product candidates from these programs is highly uncertain and may not result in approved products. Completion dates and completion costs can vary significantly for each future product candidate and are difficult to predict. We anticipate we will make determinations as to which product candidates to pursue and how much funding to direct to each product candidate on an ongoing basis in response to our ability to maintain or enter into collaborations with respect to each product candidate, the scientific and clinical success of each product candidate as well as ongoing assessments as to the commercial potential of product candidates. We will need to raise additional capital and may seek additional collaborations in the future in order to advance our various product candidates. Additional private or public financings may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a material adverse effect on our financial condition and our ability to pursue our business strategy.

### ***General and administrative expenses***

General and administrative expenses consist primarily of salaries and related benefits, including stock-based compensation, related to our executive, finance, legal, business development and support functions. Other general and administrative expenses include travel expenses, professional fees for legal, audit, tax and other professional services

and allocated facility-related costs not otherwise included in research and development expenses.

***Interest income***

Interest income consists of interest income earned on our cash and cash equivalents, held-to-maturity investments and assets held in restriction.

**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 condensed consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the U.S.

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(GAAP) and in accordance with the rules and regulations of the SEC. The preparation of these condensed 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 condensed 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, revenue recognition, deferred revenues and stock-based compensation. 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 10, 2016. There have been no material changes to our critical accounting policies during the three or nine month periods ended September 30, 2016 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 10, 2016.

**Recent Accounting Pronouncements**

***Stock Compensation***

In March 2016, the FASB issued ASU No. 2016-09, Compensation - Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting. The new standard 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 on the statement of cash flows. The new standard will be effective for us on January 1, 2017. We are currently evaluating the potential impact that this standard may have on our financial position, results of operations and statement of cash flows.

***Leases***

In February 2016, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) No. 2016-02, Leases (Topic 842). The ASU requires lessees to put most leases on their balance sheets as a liability for the obligation to make lease payments and as a right-of-use asset, but recognize expenses on the income statements in a manner similar to today's accounting. The guidance also eliminates the current real estate-specific provisions for all entities. For calendar-year public entities, the guidance becomes effective in 2019 and interim periods within that year. Early adoption is permitted for all entities. The Company has not chosen early adoption for this ASU and is currently evaluating its effect on the Company's consolidated financial statements.

***Income Taxes***

In November 2015, the FASB issued ASU No. 2015-17, Income Taxes (Topic 740): Balance Sheet Classification of Deferred Taxes. ASU No. 2015-17 simplifies the presentation of deferred income taxes by eliminating the separate classification of deferred income tax assets and liabilities into current and noncurrent amounts in the consolidated balance sheet statement of financial position. The amendments in the update require that all deferred tax assets and liabilities be classified as noncurrent in the consolidated balance sheet. The amendments in this update are effective for annual periods beginning after December 15, 2017, and interim periods therein and may be applied either

prospectively or retrospectively to all periods presented. Early adoption is permitted. The Company has early adopted this standard in the fourth quarter of 2015 on a prospective basis, and it did not have an effect on the Company's consolidated financial statements.

**Table of Contents****Going Concern**

In August 2014, the FASB issued ASU No. 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*. ASU No. 2014-15 provides guidelines for determining when and how to disclose going concern uncertainties in the financial statements. The new standard requires management to perform interim and annual assessments of an entity's ability to continue as a going concern within one year of the date the financial statements are issued. An entity must provide certain disclosures if conditions or events raise substantial doubt about the entity's ability to continue as a going concern. ASU 2014-15 is effective for the Company for annual periods ending after December 15, 2016, and interim periods thereafter, with early adoption permitted. The adoption of ASU 2014-15 is not expected to have a material impact on the Company's consolidated financial statements.

**Revenue Recognition**

In May 2014, the FASB issued ASU No. 2014-09, Revenue from Contracts with Customers (Topic 606). ASU No. 2014-09 amends the guidance for accounting for revenue from contracts with customers. This ASU supersedes the revenue recognition requirements in Accounting Standards Codification Topic 605, Revenue Recognition, and creates a new Topic 606, Revenue from Contracts with Customers. This guidance was originally pronounced to become effective for fiscal years beginning after December 15, 2016, with early adoption not permitted. On July 9, 2015, the FASB decided to defer the effective date of the ASU by one year. As a result, the Company will be required to apply the new revenue standard to annual reporting periods beginning after December 15, 2017, and would be permitted to adopt the ASU early, but not before the original public organization effective date (annual periods beginning after December 15, 2016). Two adoption methods are permitted: retrospectively to all prior reporting periods presented, with certain practical expedients permitted; or retrospectively with the cumulative effect of initially adopting the ASU recognized at the date of initial application. The Company has not yet determined which adoption method it will utilize or the effect, if any, the adoption of this guidance will have on its consolidated financial statements through December 31, 2015 as the Company has yet to record revenue from contracts with customers.

**Comparison of Three and Nine Month Periods Ended September 30, 2016 and 2015**

The following table summarizes the results of our operations for the periods indicated (in thousands):

|                            | THREE MONTHS ENDED<br>SEPTEMBER 30, |          |                        | NINE MONTHS ENDED<br>SEPTEMBER 30, |          |                        |
|----------------------------|-------------------------------------|----------|------------------------|------------------------------------|----------|------------------------|
|                            | 2016                                | 2015     | Increase<br>(Decrease) | 2016                               | 2015     | Increase<br>(Decrease) |
| Revenue                    | \$ 162                              | \$       | \$ 162                 | \$ 162                             | \$ 184   | \$ (22)                |
| Expenses:                  |                                     |          |                        |                                    |          |                        |
| Research and development   | 10,061                              | 12,142   | (2,081)                | 32,357                             | 32,708   | (351)                  |
| General and administrative | 4,338                               | 4,857    | (519)                  | 13,478                             | 14,822   | (1,344)                |
| Total expenses             | 14,399                              | 16,999   | (2,600)                | 45,835                             | 47,530   | (1,695)                |
| Loss from operations       | (14,237)                            | (16,999) | 2,762                  | (45,673)                           | (47,346) | 1,673                  |
| Interest income            | 61                                  | 55       | 6                      | 182                                | 142      | 40                     |

|          |             |             |          |             |             |          |
|----------|-------------|-------------|----------|-------------|-------------|----------|
| Net loss | \$ (14,176) | \$ (16,944) | \$ 2,768 | \$ (45,491) | \$ (47,204) | \$ 1,713 |
|----------|-------------|-------------|----------|-------------|-------------|----------|

*Revenue*

In April 2015, the National Cancer Institute (NCI), a division of the National Institutes of Health (NIH), awarded us a grant related to cancer treatment research. The project period for this grant covered a six month period which commenced in April 2015, with total funds available of approximately \$0.2 million. The payment of the NIH grant award was based upon subcontractor and internal costs incurred that are specifically covered by the grant, and where applicable, a facilities and administrative rate that provides funding for overhead expenses. In August 2016, the NCI awarded an additional \$2 million for a second phase of the grant covering the period September 1, 2016 to February 28, 2018. Of this amount, \$1 million is committed funding and the additional funding commitment is expected in the third quarter of 2017, subject to NCI approval and availability of funds. The Company recognized zero and \$0.2 million of revenue associated with the NIH grant awards for the three and nine month periods ended September 30, 2015, respectively, and \$0.1 million of revenue for the three and nine month periods ended September 30, 2016.

We do not expect to generate any product revenue for the foreseeable future.

**Table of Contents***Research and development expenses*

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

|                                             | <b>THREE MONTHS ENDED<br/>SEPTEMBER 30,</b> |                  |           | <b>Increase<br/>(Decrease)</b> |
|---------------------------------------------|---------------------------------------------|------------------|-----------|--------------------------------|
|                                             | <b>2016</b>                                 | <b>2015</b>      |           |                                |
| Direct research and development expenses    | \$ 3,105                                    | \$ 4,232         | \$        | (1,127)                        |
| Platform-related expenses                   | 3,254                                       | 4,221            |           | (967)                          |
| Employee-related expenses                   | 2,912                                       | 2,826            |           | 86                             |
| Facilities, depreciation and other expenses | 790                                         | 863              |           | (73)                           |
| <b>Total</b>                                | <b>\$ 10,061</b>                            | <b>\$ 12,142</b> | <b>\$</b> | <b>(2,081)</b>                 |

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Research and development expenses were \$10.1 million for the three month period ended September 30, 2016 ( the 2016 Quarter ), as compared to \$12.1 million for the three months ended September 30, 2015 ( the 2015 Quarter ). Direct research and development expenses were \$3.1 million for the 2016 Quarter compared to \$4.2 million for the 2015 Quarter. The decrease of \$1.1 million is due to a decrease in manufacturing and toxicology testing activities, partially offset by an overall increase in clinical activities from initiating additional sites and enrolling patients in our clinical trials. Platform-related expenses were \$3.2 million for the 2016 Quarter compared to \$4.2 million for the 2015 Quarter. The decrease of \$1.0 million is due to lower spending in discovery and early development as programs have advanced year over year into manufacturing and clinical testing, partially offset by additional pre-clinical studies for our new GalXC platform in 2016. Employee-related expenses and facilities, depreciation and other expenses have remained consistent between the 2016 Quarter and the 2015 Quarter.

|                                             | <b>NINE MONTHS ENDED<br/>SEPTEMBER 30,</b> |                  |                                |
|---------------------------------------------|--------------------------------------------|------------------|--------------------------------|
|                                             | <b>2016</b>                                | <b>2015</b>      | <b>Increase<br/>(Decrease)</b> |
| Direct research and development expenses    | \$ 10,330                                  | \$ 12,255        | \$ (1,925)                     |
| Platform-related expenses                   | 9,257                                      | 9,998            | (741)                          |
| Employee-related expenses                   | 10,075                                     | 8,308            | 1,767                          |
| Facilities, depreciation and other expenses | 2,695                                      | 2,147            | 548                            |
| <b>Total</b>                                | <b>\$ 32,357</b>                           | <b>\$ 32,708</b> | <b>\$ (351)</b>                |

Research and development expenses were \$32.4 million for the nine month period ended September 30, 2016 ( the 2016 Period ), as compared to \$32.7 million for the nine months ended September 30, 2015 ( the 2015 Period ). Direct research and development expenses were \$10.3 million for the 2016 Period compared to \$12.2 million for the 2015 Period. The decrease of \$1.9 million is due to a decrease in manufacturing, and toxicology testing activities, partially offset by an overall increase in clinical activities from initiating additional sites and enrolling patients in our clinical trials during 2016. Platform-related expenses were \$9.3 million for the 2016 Period compared to \$10.0 million for the 2015 Period. The \$0.7 million decrease was primarily due to lower spending in discovery and early development as programs have advanced year over year into manufacturing and clinical testing, partially offset by additional pre-clinical studies for our new GalXC platform in 2016. Employee-related expenses were \$10.1 million for the 2016 Period compared to \$8.3 million for the 2015 Period. The increase of \$1.8 million was primarily due to an increase in headcount and an increase in stock-based compensation of \$0.6 million. Facilities, depreciation and other expenses have increased by \$0.5 million for the 2016 Period compared to the 2015 Period due to increased occupancy costs. We expect our research and development expenses to decrease over the next few months as the clinical development programs for DCR-PH1 and DCR-MYC wind down.

*General and administrative expenses*

General and administrative expenses were \$4.3 million for the 2016 Quarter compared to \$4.9 million for the 2015 Quarter. The decrease in the 2016 Quarter was due to a decrease in stock-based compensation of \$0.4 million and a decrease of \$0.1 million in other general and administrative expenses. For the 2016 Period, general and administrative expenses were \$13.5 million compared to \$14.8 million for the 2015 Period. The decrease in the 2016 Period was primarily due to a decrease in stock-based compensation of \$0.7 million and a decrease of \$0.6 million in travel, occupancy and other general and administrative expenses.

We expect general and administrative expenses to increase in the future as we continue to expand our operating activities and incur additional costs associated with being a publicly-traded company. These increases will likely include legal, accounting and other professional services costs, directors' and officers' liability insurance premiums and costs associated with investor relations.

#### *Interest income*

Interest income in both quarters and periods was generated from the Company's money market accounts and held-to-maturity investments.

### **Liquidity and Capital Resources**

Since our inception and through September 30, 2016, we have raised an aggregate of \$266.9 million to fund our operations, of which approximately \$45.4 million was from the May 2015 follow-on offering of common stock, \$0.3 million was from a federal government grant from the NIH covering our work on cancer treatment research, \$92.7 million was from the initial public offering of our common stock, which closed on February 4, 2014, \$110.5 million was from the sale of preferred stock and convertible debt securities (including \$3.0 million from the 2013 bridge note financing), \$17.5 million was through our collaboration and license

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agreement with KHK and \$0.5 million was from a federal government grant for our Qualifying Therapeutic Discovery Project in November 2010. As of September 30, 2016, we had cash and cash equivalents and held-to-maturity investments of \$57.5 million and we also had \$1.1 million in assets held in restriction.

Contemporaneously with the filing of our Form 10-K on March 12, 2015, we filed with the SEC a universal shelf registration statement on Form S-3 permitting the sale of 10,000,000 shares of our common stock and \$50.0 million of other securities.

On May 27, 2015, we closed a follow-on offering of 2,750,000 shares of common stock, under our shelf registration statement, at a price to the public of \$17.75 per share, resulting in net proceeds to the Company of \$45.4 million after deducting underwriting discounts and commissions of approximately \$2.9 million and costs of the offering of approximately \$0.4 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.

In addition to our existing cash and cash equivalents, for each product candidate under our research collaboration and license agreement with KHK, we are entitled to receive clinical, regulatory and commercialization milestone payments of up to \$110.0 million and royalties on net sales of such product candidate. Our ability to earn these milestone payments and the timing of achieving these milestones is dependent upon the outcome of our research and development and regulatory activities and is uncertain at this time. Our right to receive the payment of certain milestones under our agreement with KHK is our only committed external source of funds.

***Cash flows***

As of September 30, 2016, we had \$57.5 million in cash and cash equivalents and held-to-maturity investments and \$1.1 million in assets held in restriction.

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

|                                                  | <b>NINE MONTHS ENDED<br/>SEPTEMBER 30,</b> |             |                   |
|--------------------------------------------------|--------------------------------------------|-------------|-------------------|
|                                                  | <b>2016</b>                                | <b>2015</b> | <b>Difference</b> |
| Net cash used in operating activities            | \$ (37,157)                                | \$ (35,529) | \$ (1,628)        |
| Net cash provided by in investing activities     | 13,109                                     | 16,639      | (3,530)           |
| Net cash provided by financing activities        | 534                                        | 45,766      | (45,232)          |
| (Decrease) increase in cash and cash equivalents | \$ (23,514)                                | \$ 26,876   | \$ (50,390)       |

***Operating activities***

Net cash used in operating activities was \$37.1 million and \$35.5 million for the 2016 Period and 2015 Period, respectively. The \$1.6 million increase in cash used in operating activities reflects a \$1.7 million decrease in our net loss, offset by changes in working capital totaling \$3.1 million and a \$0.2 million decrease in non-cash items.

*Investing activities*

Net cash provided by investing activities was \$13.9 million and \$16.6 million for the 2016 Period and 2015 Period, respectively. The decrease in net cash provided by investing activities of \$3.5 million was primarily due to the mix of purchases and maturities of investments held-to-maturity resulting in a decrease of \$3.9 million offset by a decrease in purchases of property and equipment of \$0.6 million.

*Financing activities*

Net cash provided by financing activities was \$0.5 million and \$45.8 million for the 2016 Period and the 2015 Period, respectively. In 2015, net proceeds from our follow-on offering of common stock was approximately \$45.4 million.

*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 trade secret misappropriation claim against us, and general overhead costs. Because of the

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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 increased capital outlays and operating expenditures associated with our current and anticipated development activities. However, based on our current operating plan, we continue to believe that our cash and cash equivalents, excluding any potential option exercise fees or milestone payments, will be sufficient to meet our anticipated cash requirements for at least the next twelve months. 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 research collaboration and license agreement with 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 progress, costs and results of our preclinical studies and clinical trials;

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 (see Legal Proceedings);

the costs and timing of procuring clinical and commercial supplies of 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 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 may cause us to reduce our headcount or reduce spending on our clinical and pre-clinical programs and the development of our product candidates.

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, 2016 (in thousands):

| CONTRACTUAL OBLIGATIONS                 | TOTAL    | PAYMENTS DUE BY PERIOD |                              |                                         |                   |
|-----------------------------------------|----------|------------------------|------------------------------|-----------------------------------------|-------------------|
|                                         |          | LESS THAN 1 YEAR       | 1 YEAR AND LESS THAN 3 YEARS | MORE THAN 3 YEARS AND LESS THAN 5 YEARS | MORE THAN 5 YEARS |
| Existing operating lease obligations(1) | \$ 6,857 | \$ 1,570               | \$ 3,284                     | \$ 2,003                                | \$                |

- (1) Total commitments includes future minimum lease payments under our existing non-cancelable operating lease for our office and laboratory space in Cambridge, Massachusetts, as executed on July 11, 2014 with an average rent of approximately \$0.1 million per month.

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We also have obligations to make future payments to COH, and PBL that become due and payable on the achievement of certain development, regulatory and commercial milestones. We have not included these commitments on our balance sheet or in the table above because the achievement and timing of these milestones is not probable and estimable.

## **Off-balance Sheet Arrangements**

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in Item 303 of Regulation S-K of the rules and regulations of the Securities and Exchange Commission.

## **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, 2016, we had cash and cash equivalents and held-to-maturity investments of \$57.5 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 and 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, government and non-government debt securities and corporate obligations.

## **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 Securities Exchange Act of 1934, as amended (Exchange Act), with the Securities and Exchange Commission (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, 2016, which was identified in connection with our management's evaluation required by Exchange Act Rules 13a-15(f) and 15d-15(f) 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.

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**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 Pharmaceuticals, Inc. (Alnylam) filed a complaint against the Company in the Superior Court of Middlesex County, Massachusetts. 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, damages, attorneys' fees, and an order permanently enjoining the Company from disclosing or using any of Alnylam's confidential information or trade secrets. This matter could potentially cause us to incur significant additional legal fees and other costs to defend this action, and 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. We believe, however, that Alnylam's allegations lack merit. We have filed an answer denying all liability, and we intend to 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.

**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 (Exchange Act), and Section 27A of the Securities Act of 1933, as amended (Securities Act). 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 with other organizations to provide these capabilities for us. 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 that are approved for commercial sale. As of September 30, 2016, we had \$57.5 million in cash and cash equivalents and held-to-maturity investments.

Based on our current operating plan, 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 next 12 months. 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;

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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 obtain regulatory approvals;

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 in general.

If we are unable to obtain funding on a timely basis or on acceptable terms, 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 primarily financed our operations through the sale of securities, debt financings, credit and loan facilities and payments received under our collaborations and license agreement with Kyowa Hakko Kirin Co., Ltd. (KHK). 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. 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. Our failure to raise capital or enter into such other arrangements within 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, pre-clinical or clinical trials or undergo reductions in our workforce or other corporate restructuring activities.

***We are a clinical stage 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 clinical stage biopharmaceutical company with a limited operating history, focused on the discovery and development of treatments based on the emerging therapeutic modality RNA interference (RNAi), a biological process in which ribonucleic acid (RNA) molecules inhibit gene expression. Since our inception in October 2006, we have devoted our resources to the development of Dicer substrate RNA (DsiRNA) molecules and delivery

technologies. We have had significant operating losses since our inception. As of September 30, 2016, we had an accumulated deficit of \$241.7 million. For the nine months ended September 30, 2016 and the years ended December 31, 2015, 2014 and 2013, our net loss was \$45.5 million, \$62.8 million, \$47.9 million and \$18.5 million, respectively. Substantially all of our losses have resulted from expenses incurred in connection with our research 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.

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***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 licensing partner;

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 lawsuit or opposition, interference, re-examination, post-grant review, inter partes review, nullification, derivation action, or cancellation proceeding in which we may become involved;

additions and departures of key personnel;

strategic decisions by us or 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;

expenditures as we respond to and defend against complaints and potential litigation, including Alnylam's lawsuit alleging misappropriation of confidential information; and

changes in general market and economic conditions.

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

***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, 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 based on the therapeutic modality RNAi and the identification and optimization of GalXC is relatively new. Further, 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 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.

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Further, the U.S. Food and Drug Administration (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 could 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 factors such as whether the product can be sold at a competitive cost and otherwise 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 to accept and use, or to provide favorable 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 patients to accept any new methods of administration;

the success of our physician education programs;

the availability of adequate government and third-party payor reimbursement;

the pricing of our products, particularly as compared to alternative treatments; 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 space becomes more competitive or less favored in the commercial marketplace. Additional risks apply in relation 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 European Union 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 not classified as rare. Our estimates regarding potential market size for any indication may be materially different from what we discover to exist at the time we commence commercialization, if any, for a product, 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 which it has such 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.

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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 European Union before the application for marketing authorization is made. Sponsors of orphan drugs in the European Union 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.

***Our product candidates are in early stages of development and may fail in development or suffer delays that materially 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 institutional review board (IRB) 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 or 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 scientific feasibility, safety, efficacy, changing standards of medical care and other variables. 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, 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 subjects 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 INDs 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 research subjects in clinical trials;

high drop-out rates of research subjects;

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; or

varying interpretations of data by the FDA and similar foreign regulatory agencies.

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***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 the research collaboration and license agreement with KHK, 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. The success of our collaboration programs with KHK depends entirely upon the efforts of KHK. 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 may not be effective in obtaining approvals for the product candidates developed under the collaboration arrangement or in marketing, or arranging for necessary supply, manufacturing or distribution relationships for, any approved products. Under the research collaboration and license agreement, KHK may change its strategic focus or pursue alternative technologies in a manner that results in reduced, delayed or no revenue to us. KHK has a variety of marketed products and product candidates under collaboration with other companies, including some of our competitors, and its own corporate objectives may not be consistent with our best interests. If KHK fails to develop, obtain regulatory approval for or ultimately commercialize any product candidate under our collaboration or if KHK terminates our collaboration, our business, financial condition, results of operations and prospects could be materially and adversely affected. In addition, any dispute or litigation proceedings we may have with KHK in the future 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 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 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. The FDA and certain foreign regulatory authorities, such as the European Medicines Agency (EMA), require preclinical studies to be conducted in accordance with applicable Good Laboratory Practices (GLPs) and clinical trials to be conducted in accordance with applicable FDA regulations and good clinical practices (GCPs), 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 partners to supply the materials, components and manufacturing services for our research and development, preclinical study and clinical trial drug supplies.

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We do not own 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 products to patients, we may lose patients, physicians may elect to utilize competing therapeutics instead of our products, and our trials may be adversely affected, which could materially and adversely affect our 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 (cGMPs). In the event that any of our suppliers or manufacturers fails to comply with such requirements or to perform its obligations to us in relation to 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, City of Hope, Carnegie Institution of Washington, Plant Bioscience Limited and Arbutus, 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 candidate 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

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business. These transactions would 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 will develop product candidates and processes competitive with 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 multiple 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 in March 2014 acquired Sirna Therapeutics, Inc. from Merck & Co., Inc., Arbutus, with which we have license and development and supply agreements, 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 City of Hope (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 pre-clinical 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. There are also competitors to our proprietary product candidates currently in development, some of which may become commercially available before our product candidates.

We also compete with companies working to develop antisense and other RNA-based drugs. Like RNAi therapeutics, antisense drugs target messenger RNA (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 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, Pankaj Bhargava, M.D., our chief medical officer, Bob D. Brown, Ph.D., our chief

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scientific 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 technical 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 did not begin our first clinical trial of a product candidate until 2014. 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 or partners, 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 is 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 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 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 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 European Union, 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, and import and export of pharmaceutical products. 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 strategies (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

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new information becomes available. In addition, the relevant governmental authority of any European Union 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 and total or partial suspension of production or distribution, injunction, restitution, disgorgement, debarment, civil penalties and criminal prosecution.

We have a legal entity physically located in the United Kingdom (U.K.), which we established in order to conduct clinical trials in EU member states. On June 23, 2016, the U.K. held a referendum in which voters approved an exit from the E.U., commonly referred to as Brexit. The withdrawal of the United Kingdom from the European Union will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the United Kingdom provides a notice of withdrawal pursuant to the EU Treaty. No announcement has been made by the U.K. government as to when it intends to deliver any notice of withdrawal. It appears likely that this withdrawal will involve a process of lengthy negotiations between the United Kingdom and European Union member states to determine the future terms of the United Kingdom's relationship with the European Union. This could lead to a period of considerable uncertainty and could impact our regulatory process in Europe.

***Price controls imposed in foreign markets may adversely affect our future profitability.***

In some countries, particularly member states of the European Union, 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, 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 European Union 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 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 the related litigation, a diversion of management's time and our resources, substantial monetary awards to 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.

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***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 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 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 programs 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 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.***

Despite the implementation of security measures, our internal computer systems and those of 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. 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, 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 with our partners 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

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accidents or incidents that result in us being unable to fully utilize 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. As of December 31, 2015, we had U.S. federal and Massachusetts net operating loss carryforwards of \$92.5 million and \$77.6 million, respectively. 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, 2016, we had \$57.5 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, including the impact of U.S. sub-prime mortgage defaults that have 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 Securities and Exchange Commission and the Public Company Accounting Oversight Board. Changes to accounting methods or policies, or interpretations thereof, may require us to reclassify, restate or otherwise change or revise our financial statements, including those contained in our Annual Report on Form 10-K for the year ended December 31, 2015.

### **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 October 10, 2016, our worldwide patent estate, not including the patents and patent applications that we have licensed, included over 20

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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 try 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 (AIA) 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 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 will 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.

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.

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***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 an exclusive or non-exclusive basis. 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 products 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 products or the use of our products. 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.

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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. In addition, we have an exclusive worldwide license from Arbutus to their LNP technology for delivery of certain therapeutics to treat PH1, and Arbutus retains ownership of its patents. This technology could be important to us if we resume clinical development of DCR-PH1. 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 or any future strategic partners. 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

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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 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. Competitor products may compete with our future products 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 European Union, 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 in some jurisdictions be refused by the relevant registration authorities, while granted by others. It is also quite common that 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 or our licensors, collaborators or any future strategic partners 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 or our licensors, collaborators or any future strategic partners 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 or our licensors, collaborators or any future strategic partners 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 or our licensors, collaborators or any future strategic partners 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 or our collaborator, or any future collaborator, 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.

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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 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 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, 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.

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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 Pharmaceuticals, Inc. 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 Therapeutics, Inc., or Sirna, which at the time was a subsidiary of Merck & Co., Inc., 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 of our employees 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. 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, then 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 partners 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, unable to commercialize our product candidates.***

Our product candidates are subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, approval, recordkeeping, reporting, labeling, storage, packaging, advertising and promotion, pricing, marketing, sampling, and distribution 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 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, 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 authority also may impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or

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efficacy of the product. In addition, the FDA has the authority to require a Risk Evaluation and Mitigation Strategy (REMS) plan as part of an NDA or biologics license application (BLA) 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 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 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 law, 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 law, 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 Federal Food, Drug and Cosmetic Act 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;

the U.S. federal Health Insurance Portability and Accountability Act (HIPAA) and Health Information Technology for Economic and Clinical Health (HITECH) Act, 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 Open Payments regulations under the National Physician Payment Transparency Program have been issued under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, and will require that manufacturers of pharmaceutical and biological drugs covered by Medicare, Medicaid, and Children's Health Insurance Programs report all consulting fees, travel reimbursements, research grants, and other payments or gifts with values over \$10 made to physicians and teaching hospitals; and

state laws comparable to each of the above federal laws, such as, for example, anti-kickback and false claims laws applicable to commercial insurers and other non-federal payors, requirements for mandatory corporate regulatory compliance 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. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time and resources.

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If we or our collaborators, manufacturers or service providers fail to comply with applicable federal, state or foreign 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;

exclusion from participation in government-funded healthcare programs;

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 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 or the likely level or method of reimbursement. 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. 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.

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Under current law, as a condition of receiving Medicare Part B reimbursement 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 (MDRP) and the 340B Drug Discount 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 drugs are typically reimbursed under Medicare Part D, and drugs that are administered in a 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., Congress passed the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (ACA), which 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 Discount 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.

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, 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.

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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. 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 False Claims Act), prohibit unlawful inducements for the referral of business reimbursable by federal healthcare programs (e.g. the Anti-Kickback Statute), and require disclosure of certain payments or other transfers of value made to U.S.-licensed physicians and teaching hospitals (the Physician Payments Sunshine Act). 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, the Health Insurance Portability and Accountability Act of 1996 (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, the Company may also be subject to the privacy and security provisions of HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, 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.***

U.S. federal government agencies currently face potentially significant spending reductions. The Budget Control Act of 2011 (BCA) established a Joint Select Committee on Deficit Reduction, which was tasked with achieving a reduction in the federal debt level of at least \$1.2 trillion. That committee did not draft a proposal by the BCA's deadline. As a result, automatic cuts (sequestration) in various federal programs were scheduled to take place, beginning in January 2013, although the American Taxpayer Relief Act of 2012 delayed the BCA's automatic cuts until March 1, 2013. While the Medicare program's eligibility and scope of benefits are generally exempt from these cuts, Medicare payments to providers and Part D health plans are not exempt. The BCA did, however, provide that the Medicare cuts to providers and Part D health plans would not exceed two percent. President Obama issued the

sequestration order on March 1, 2013, and cuts went into effect on April 1, 2013. Additionally, the Bipartisan Budget Act of 2013 extended sequestration for Medicare for another two years, through 2023, and a bill signed by the President on February 15, 2014, further extended these cuts for an additional year, through fiscal year 2024. On January 21, 2014, President Obama signed the fiscal year 2014 omnibus appropriations bill, modifying for fiscal year 2014 and fiscal year 2015 the cuts that went into effect under the sequester on March 1, 2013.

The situation with the federal budget remains in flux. From October 1, 2013 through October 16, 2013, the U.S. federal government ceased the majority of its operations after Congress failed to enact legislation appropriating funds for fiscal year 2014. On October 17, 2013, President Obama signed into law the Continuing Appropriations Act of 2014, which included a continuing resolution to fund the government until January 15, 2014 and suspended the statutory debt ceiling until February 7, 2014. After extending the government funding expiration date to January 18, 2014, Congress passed a \$1.1 trillion spending bill that was signed into law on January 17, 2014 and funds the government through September 30, 2014. While on December 9, 2014, Congress passed the Consolidated and Further Continuing Appropriations Act of 2015, which funds the government through September 30, 2015, this new law is a temporary measure that does not resolve the debt-limit issue. Many Members of Congress have made public statements indicating that some or all of these budget-related deadlines should be used as leverage to negotiate additional cuts in federal spending. 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 would be uncertain. If federal spending is reduced, anticipated budgetary shortfalls may also impact the ability of relevant

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agencies, such as the FDA or the National Institutes of Health 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 receives 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 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 we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors.***

We are an emerging growth company as defined in the Jumpstart Our Business Act (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 any June 30 before that time 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 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.

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***Our stock price may be 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 9, 2016, our stock had high and low closing sale prices in the range of \$46.00 and \$2.70 per share. The market price for our common stock may drop significantly as a result of many factors, including the other risks described in this section titled "Risk Factors" 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 products;

introductions and announcements of new products by us, our commercialization partners, or our competitors, and the timing of these introductions or announcements;

actions taken by regulatory agencies with respect to our or our competitors' 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 partnerships, 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 in connection with the follow-on public offering of our common stock with the holders of substantially all of our outstanding shares;

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.



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In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that has been often 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 us, 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 us, 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, 2016, our executive officers and directors, together with holders of five percent or more of our outstanding common stock and their respective affiliates, beneficially own, in the aggregate, approximately 50.0 percent of our outstanding common stock, including shares 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 certificate of incorporation and our 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,

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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 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, 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 (Section 404(b)), and are therefore not required to make a formal assessment of the effectiveness of our internal control over financial reporting for that purpose. Pursuant to Section 404(b), we will be required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth 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(b) 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(b). 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 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 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

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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 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. As of November 4, 2016, 579,715 shares of common stock were reserved for future issuance under our stock incentive plans. As of that date, there were also stock options and awards to purchase 5,192,354 shares of our common stock outstanding and warrants to purchase 87,901 shares of our common stock outstanding. The exercise price of outstanding options or warrants having an exercise price per share 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 4, 2016, we have 20,753,001 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.

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

***(a) Unregistered Sales of Equity Securities***

We did not have any unregistered sales of equity securities during the period covered by this report.

***(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.

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**Item 3. DEFAULTS UPON SENIOR SECURITIES**

Not applicable.

**Item 4. MINE SAFETY DISCLOSURES**

Not applicable.

**Item 5. OTHER INFORMATION**

*Amendment to Employment Agreement*

On November 4, 2016, the compensation committee of our board of directors approved an amended and restated employment agreement with John B. Green, our chief financial officer. The amended and restated employment agreement was entered into on November 4, 2016. The amended and restated employment agreement retains all of the prior terms except that it provides for full acceleration of the vesting of Mr. Green's equity in the event of a change of control.

The foregoing description of the terms of the amended and restated employment agreement does not purport to be complete and is qualified in its entirety by reference to the full text of the employment agreements, a copy of which is filed herewith.

**Table of Contents****Item 6. EXHIBITS****Exhibit**

| <b>Number</b> | <b>Description of Documents</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|---------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 10.1(1)       | Amended and Restated Employment Agreement by and between the Company and <u>Douglas M. Fambrough, III</u> ++                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| 10.2(1)       | Amended and Restated Employment Agreement by and between the Company and <u>Bob. D. Brown</u> ++                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| 10.3(1)       | Amended and Restated Employment Agreement by and between the Company and <u>James B. Weissman</u> ++                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| 10.4(1)       | Amended and Restated Employment Agreement by and between the Company and <u>John B. Green</u> ++                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| 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, 2016, formatted in XBRL (eXtensible Business Reporting Language), include: (i) the Condensed Consolidated Balance Sheets as of September 30, 2016 (unaudited) and December 31, 2015, (ii) the Condensed Consolidated Statements of Operations (unaudited) for the nine months ended September 30, 2016 and 2015, (iii) the Condensed Consolidated Statements of Cash Flows (unaudited) for the nine months ended September 30, 2016 and 2015, and (iv) the Notes to Condensed Consolidated Financial Statements (unaudited). |

++ Management contract or compensatory plan or arrangement.

\* Exhibit 32.1 is being furnished and shall not be deemed to be filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (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 of 1933, as amended (Securities Act), or the Exchange Act, except as otherwise stated in such filing.

(1) Filed herewith.

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**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 7, 2016

By: /s/ John B. Green

**John B. Green**

**Chief Financial Officer (Principal Financial  
Officer and Principal Accounting Officer)**

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**EXHIBIT INDEX**

**Exhibit**

**Number**

**Description of Documents**

|         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
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