Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

Form 10-K

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

For the fiscal year ended December 31, 2017

or

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

For the transition period from to

Commission File Number: 001-36281

DICERNA PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

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

87 Cambridgepark Drive Cambridge, MA 02140
(Address of principal executive offices and zip code)
(617) 621-8097
(Registrant's telephone number, including area code)

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

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock, $0.0001 par value	**The NASDAQ Global Select Market**

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

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

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

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

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

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

Based on the closing price of the registrant's Common Stock on the last business day of the registrant's most recently completed second fiscal quarter, which was June 30, 2017, the aggregate market value of its shares (based on a closing price of $3.17 per share) held by non-affiliates was approximately $30.8 million. Shares of the registrant's Common Stock held by each executive officer and director and by each entity or person that owned five percent or more of the registrant's outstanding Common Stock were excluded in that such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of March 7, 2018, there were 51,766,999 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2018 Annual Meeting of Stockholders are incorporated by reference into Part III hereof. Such proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

DICERNA PHARMACEUTICALS, INC.

2017 ANNUAL REPORT ON FORM 10-K

TABLE OF CONTENTS

Forward-Looking Statements

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

- how long we expect to maintain liquidity to fund our planned level of operations and our ability to obtain additional funds for our operations;
- the initiation, timing, progress and results of our research and development programs, preclinical studies, any clinical trials and Investigational New Drug application ("IND"), Clinical Trial Application ("CTA"), New Drug Application ("NDA") and other regulatory submissions;
- our ability to identify and develop product candidates for treatment of additional disease indications;
- our or a collaborator's ability to obtain and maintain regulatory approval of any of our product candidates;
- the rate and degree of market acceptance of any approved product candidates;
- the commercialization of any approved product candidates;
- our ability to establish and maintain additional collaborations and retain commercial rights for our product candidates in the collaborations;
- the implementation of our business model and strategic plans for our business, technologies and product candidates;
- our estimates of our expenses, ongoing losses, future revenue and capital requirements;
- our ability to obtain and maintain intellectual property protection for our technologies and product candidates and our ability to operate our business without infringing the intellectual property rights of others;
- our reliance on third parties to conduct our preclinical studies or any clinical trials;
- our reliance on third-party suppliers and manufacturers 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, Boehringer Ingelheim International GmbH ("BI") 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 BI or any future arrangements with any other collaborators;
- our expectations with regard to the outcome of the litigation with Alnylam Pharmaceuticals, Inc. ("Alnylam");
- our expectations regarding the time during which we will be an emerging growth company under the Jumpstart Our Business Startups Act of 2012;
- 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 Annual Report on Form 10-K. Any forward-looking statement in this Annual Report on Form 10-K 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 Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business and the markets for certain drugs, including data regarding the estimated size of those markets, their projected growth rates and the incidence of certain medical conditions. Information that is based on estimates, forecasts, projections or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained these industry, business, market and other data from reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources. In some cases, we do not expressly refer to the sources from which these data are derived.

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

Trademarks

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

PART I

Item 1. ***Business***

Dicerna is a biopharmaceutical company focused on the discovery and development of innovative subcutaneously delivered ribonucleic acid ("RNA") interference ("RNAi")-based pharmaceuticals using our GalXC™ RNAi platform for the treatment of diseases involving the liver, including rare diseases, viral infectious diseases, chronic liver diseases, and cardiovascular diseases. Within these therapeutic areas, we believe our GalXC RNAi platform will allow us to build a broad pipeline of therapeutics 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. Our key development programs include DCR-PHXC for the treatment of primary hyperoxaluria ("PH"), currently in a phase 1 clinical trial; and undisclosed product candidate against a serious rare liver disease, currently in IND/CTA-enabling studies; and DCR-HBVS for the treatment of hepatitis B virus ("HBV"), currently in IND/CTA-enabling studies.

All of our GalXC drug discovery and development efforts are based on the therapeutic modality of RNAi, a highly potent and specific mechanism for silencing the activity of a targeted gene. In this naturally occurring biological process, double-stranded RNA molecules induce the enzymatic destruction of the messenger ribonucleic acid ("mRNA") of a target gene that contains sequences that are complementary to one strand of the therapeutic double-stranded RNA molecule. The Company's GalXC RNAi platform utilizes a particular structure of double-stranded RNA molecules configured for subcutaneous delivery to the liver. Due to the enzymatic nature of RNAi, a single GalXC molecule incorporated into the RNAi machinery can destroy hundreds or thousands of mRNAs from the targeted gene.

The GalXC RNAi platform supports Dicerna's long-term strategy to retain, subject to the evaluation of potential licensing opportunities as they may arise, a full or substantial ownership stake and to invest internally in diseases with focused patient populations, such as certain rare diseases. We see such diseases as representing opportunities that carry a relatively higher probability of success, with genetically and molecularly defined disease markers, high unmet need, a limited number of Centers of Excellence to facilitate reaching these patients, and the potential for more rapid clinical development programs. For more complex diseases with multiple gene dysfunctions and larger patient populations, we plan to pursue collaborations that can provide the enhanced scale, resources and commercial infrastructure required to maximize these prospects. Our collaborative research and license agreement with BI, entered into on October 27, 2017 (the "BI Agreement") and pursuant to which the Company and BI jointly research and develop product candidates for the treatment of nonalcoholic steatohepatitis ("NASH") using our GalXC platform, is an example of such a collaboration.

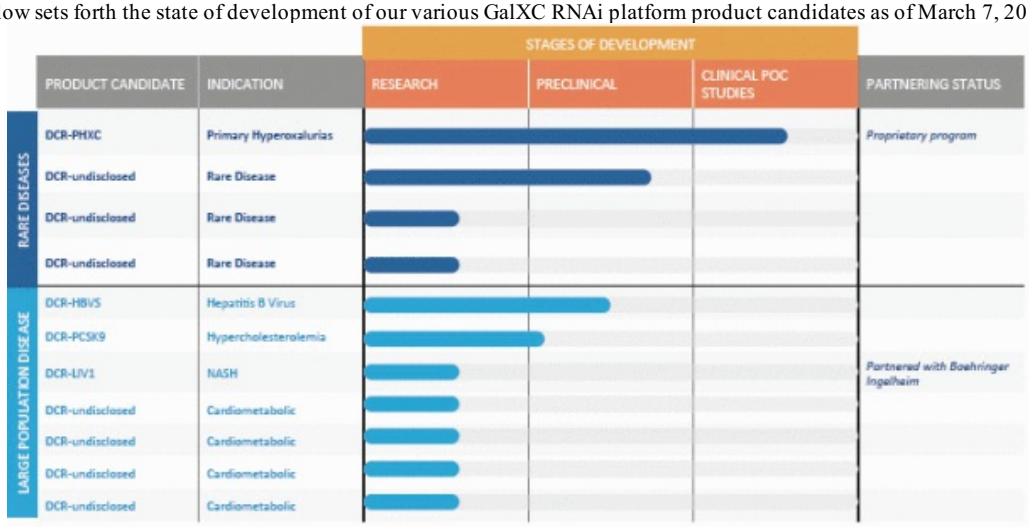
Development Programs

In choosing which development programs to advance, we apply scientific, clinical, and commercial criteria that we believe allow us to best leverage our GalXC RNAi platform and maximize value. The Company is focusing its efforts on three priority therapeutic programs that currently have a CTA filed or are in IND/CTA enabling studies and on a series of programs in the clinical candidate selection stage that may be elevated into IND/CTA enabling studies in the future, either on our own or in collaboration with larger pharmaceutical companies.

Our three priority programs are: DCR-PHXC for the treatment of primary hyperoxaluria ("PH"); a program for an undisclosed rare disease; and DCR-HBVS for the treatment of chronic hepatitis B virus ("HBV") infection. Our programs in clinical candidate selection include multiple programs targeting undisclosed targets in rare diseases, chronic liver diseases, and cardiovascular diseases including a program for the treatment of hypercholesterolemia, for which as a provisional clinical candidate, DCR-PCSK9, has already been selected. In October 2017, we filed a CTA for our lead GalXC product candidate, DCR-PHXC, with the Medicines and

Healthcare products Regulatory Agency ("MHRA") in the United Kingdom ("UK"), and in December 2017, we dosed the first human in the Phase 1 DCR-PHXC clinical trial. We expect to file additional CTAs and/or INDs for our programs in 2018 and 2019.

The table below sets forth the state of development of our various GalXC RNAi platform product candidates as of March 7, 2018.



Our current GalXC RNAi platform development programs are as follows:

- **Primary Hyperoxaluria.** We are developing DCR-PHXC for the treatment of all types of PH. PH is a family of rare inborn errors of metabolism in which the liver produces excessive levels of oxalate, which in turn causes damage to the kidneys and to other tissues in the body. Patients often endure frequent painful kidney stone events often requiring surgical intervention, and in many cases patients with PH progress to end stage renal disease. Standard of care for these patients includes intensive dialysis, and combined liver and kidney transplants. In preclinical models of PH, DCR-PHXC reduces oxalate production to near-normal levels, ameliorating the disease condition. Based on evaluation of genome sequence databases, there may be as many as 16,000 people with PH in the US and major European countries.

  On October 16, 2017, we announced that we had submitted a CTA for DCR-PHXC to the MHRA in the UK. On December 7, 2017, we announced that we dosed the first human in a Phase 1 trial of DCR-PHXC. The Phase 1 trial for DCR-PHXC, called PHYOX, is a single ascending-dose study of DCR-PHXC in normal healthy volunteers ("NHV") and patients with PH. The study is divided into two groups: Group A is a placebo-controlled, single-blind, single center Phase 1 study, enrolling up to 25 NHVs; Group B is an open-label, multi-center study enrolling up to 16 patients with PH types 1 ("PH1") and 2 ("PH2"). The primary objective of the study is to evaluate the safety and tolerability of single doses of DCR-PHXC in both groups. Secondary objectives are to characterize the pharmacokinetics of single doses of DCR-PHXC in NHVs and patients with PH, and to evaluate the pharmacodynamic effects of single doses of DCR-PHXC on biochemical markers including, but not limited to, changes in urine oxalate concentrations. Patients with PH will be dosed after safety has been established at the same dose level in normal healthy volunteers. We plan to dose the first patient in Group B in the second quarter of 2018 and expect to have clinical proof-of-concept ("POC") data in the second half of 2018. We have submitted CTAs in Germany, France and the Netherlands. Additionally,

we expect to initiate a multi-dose Phase 2/3 study in the first quarter of 2019, pending positive POC data and regulatory approvals.

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

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

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

- **An undisclosed rare disease involving the liver.** We are developing a GalXC-based therapeutic, targeting a liver-expressed gene involved in a serious rare disease. For competitive reasons, we have not yet publicly disclosed the target gene or disease. We have selected this target gene and disease based on criteria that include having a strong therapeutic hypothesis, a readily-identifiable patient population, the availability of a potentially predictive biomarker, high unmet medical need, favorable competitive positioning and what we believe is a rapid projected path to approval. The disease is a genetic disorder, where mutations in the disease gene lead to the production of an abnormal protein. The protein causes progressive liver damage and fibrosis, in some cases leading to cirrhosis and liver failure, and we believe that silencing of the disease gene will prevent production of the abnormal protein and thereby slow or stop progression of the liver fibrosis. Greater than 100,000 people in the United States ("U.S.") are believed to be homozygous (i.e. having identical pairs of genes for any given pair of hereditary characteristics) for the mutation that causes the liver disease, and at least 20% of those people, and potentially a significantly higher fraction, are believed to have liver-associated disease as a consequence. We plan to seek a risk-sharing collaborator for this program before we file an IND and/or CTA, which we expect to be prepared to file in the second quarter of 2018.
- **Chronic Hepatitis B Virus infection.** We have declared a GalXC RNAi platform-based product candidate for the treatment of HBV, DCR-HBVS, and are conducting formal non-clinical development studies. We expect to file an IND and/or a CTA during the fourth quarter of 2018. According to the World Health Organization, over 250 million people are currently living with chronic HBV infection worldwide, resulting in nearly a million deaths annually. Current therapies for HBV rarely lead to a long-term immunological cure as measured by the clearance of HBV surface antigen ("HBsAg") and sustained HBV deoxyribonucleic acid ("DNA") suppression in patient plasma or blood. DCR-HBVS targets HBV messenger RNA, and leads to greater than 99% reduction in circulated HBsAg in mouse

models of HBV infection. Based on these preclinical studies, and only if we receive appropriate regulatory approval to begin human clinical trials, we hope to determine the potential of DCR-HBVS to reduce HBsAg and HBV DNA levels in the blood of HBV patients in a subcutaneous dosing paradigm.

- **Hypercholesterolemia (PCSK9 targeted therapy).** We are using our GalXC RNAi platform to develop a therapeutic that targets the PCSK9 gene for the treatment of hypercholesterolemia. The Company has selected a provisional clinical candidate for the program, but is continuing to explore ways to further optimize the program, including exploring more advanced versions of our GalXC platform with enhanced properties, while we assess the market potential of this program. PCSK9 is a validated target for hypercholesterolemia, and there are U.S. Food and Drug Administration ("FDA")-approved therapies targeting PCSK9 that are based on monoclonal antibody technology. Based on preclinical studies, we believe that our GalXC RNAi platform has the potential to produce a PCSK9-targeted therapy with attractive commercial properties, such as small subcutaneous injection volumes and less frequent dosing.
- **Additional pipeline programs.** We have developed a robust portfolio of additional targets and diseases that we plan to pursue either on our own or in collaboration with partners. We have applied our GalXC technology to multiple gene targets across our disease focus areas of rare diseases, chronic liver diseases, and cardiovascular diseases. Pursuant to our strategy, we are seeking collaborations with larger pharmaceutical companies to advance our programs in the areas of chronic liver diseases and cardiovascular diseases. Both these disease areas represent large and diverse patient populations, requiring complex clinical development and commercialization paths that we believe can be more effectively pursued in collaboration with larger pharmaceutical companies. For our additional rare diseases, we are continuing to assess their potential for clinical success and market opportunity while optimizing our GalXC molecules. For our additional pipeline programs (including PCSK9), we may utilize more advanced versions of our GalXC technology, that further improve pharmaceutical properties of the GalXC molecules, including enhancing the duration of action and potency. Improvements to our GalXC compound include modification of the tetraloop end of the molecule, which can be applied to any target gene and program, resulting in a substantially longer duration of action in animal models across multiple targets. Modification of the tetraloop only impacts the passenger strand and does not involve any modification to the guide strand. These modifications are unique to our GalXC platform and, we believe, provide a competitive advantage for the Company.

In addition to the GalXC development programs outlined above, on October 27, 2017, we entered into the BI Agreement, pursuant to which the Company and BI jointly research and develop product candidates for the treatment of chronic liver diseases, with an initial focus on NASH, using our GalXC platform. NASH is caused by the buildup of fat in the liver, potentially leading to liver fibrosis and cirrhosis. NASH has an especially high prevalence among obese and diabetic patients, and is an area of high unmet medical need. The BI Agreement is for the development of product candidates against one target gene with an option for BI to add the development of product candidates that target a second gene. We are working exclusively with BI to develop the product candidates against the undisclosed target gene. We are responsible for the discovery and initial profiling of the product candidates, including primary pre-clinical studies, synthesis, and delivery. BI is responsible for evaluating and selecting the product candidates for further development. If BI selects one or more product candidates, it will be responsible for further pre-clinical development, clinical development, manufacturing and commercialization of those products. Also pursuant to the BI Agreement, we granted BI a worldwide license in connection with the research and development of the product candidates and will transfer to BI intellectual property rights of the product candidates selected by BI for clinical development and commercialization. We also may provide assistance to BI in order to help BI further develop selected product candidates. Pursuant to the BI Agreement, BI agreed to pay us a non-refundable upfront payment of $10.0 million for the first target. During the term of the research program, BI will reimburse us the cost of materials and third-party expenses that have been included in the preclinical studies up to an agreed-upon limit. We are eligible to receive up to $191.0 million in potential development and commercial milestones related to the initial target. We are also eligible to receive

royalty payments on potential global net sales, subject to certain adjustments, tiered from high single digits up to low double-digits. BI's option to add a second target would provide for an option fee payment and success-based development and commercialization milestones and royalty payments to us.

We are party to a collaboration for our early generation of non-GalXC Dicer Substrate 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 has provided us with notice of termination related to the non-KRAS program. We also have developed a wholly owned clinical candidate, DCR-BCAT, targeting the ß-catenin oncogene. DCR-BCAT is based on an extended version of our earlier generation non-GalXC Dicer Substrate RNAi technology and is delivered by our lipid nanoparticle ("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.

Strategy

We are committed to delivering transformative therapies based on our GalXC RNAi platform to patients with rare inherited diseases involving the liver and for other therapeutic areas involving the liver such as viral infectious diseases, chronic liver diseases, and cardiovascular diseases. We have qualified dozens of disease-associated genes in clinical indications where we believe an RNAi-based inhibitor may provide substantial benefit to patients, providing expansive therapeutic opportunities.

The key elements of our strategy are as follows.

- **Create new programs in indication areas with high unmet medical need.** We intend to continue to use our proprietary GalXC RNAi technology platform to create new, high value pharmaceutical programs. Our primary focus will remain: (1) rare inherited diseases involving genes in the liver; and (2) other therapeutic areas involving the expression of therapeutic gene targets in the liver such as viral infectious diseases, chronic liver diseases, and cardiovascular diseases.
- **Validate our product candidates and our platform in clinical proof-of-concept studies.** We intend to demonstrate clinical proof-of-concept for DCR-PHXC (which is in development for all forms of PH) and for our other development programs. Based on precedents in the RNAi field, we are optimistic that our preclinical, which show the significant knockdown of target mRNA activity lasting for up to three months after the last dose and disease biomarker activity, potentially may translate into beneficial clinical results for these programs.
- **Retain significant portions of the commercial rights for certain rare disease programs.** We seek to retain a full or substantial ownership stake and invest internally in disease areas with focused patient populations, such as certain rare diseases. We see such diseases 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.
- **Enter into additional collaborations with pharmaceutical companies either for our GalXC RNAi technology platform or specific indications or therapeutic areas.** For more complex diseases with multiple gene dysfunctions and larger patient populations, we plan to pursue collaborations that can provide the enhanced scale, resources and commercial infrastructure required to maximize these prospects, such as our collaboration with BI for the treatment of chronic liver diseases. We may choose to establish collaborations with pharmaceutical companies across multiple programs or specific indication areas, either before or after clinical proof-of-concept, depending on the attractiveness of the opportunities. These collaborations may provide us with further validation of our technology platform, funding to advance our proprietary product candidates, or access to development, manufacturing and commercial capabilities.

- **Continue to invest in our RNAi technology platform and intellectual property.** We plan to continue to invest in expanding and improving our GalXC RNAi platform technology. We believe we have a robust patent portfolio covering our proprietary GalXC RNAi platform and other RNAi technologies. As of March 7, 2018, our patent estate, not including the patents and patent applications we have licensed, included over 35 issued patents or allowed patent applications and over 100 pending patent applications supporting commercial development of our RNAi molecules and delivery technologies.
- **Leverage the experience and the expertise of our executive management team.** To execute on our strategy, we have assembled an executive management team that has extensive experience in the biopharmaceutical industry. In addition, various members of our management team and our board of directors have contributed to the progress of the RNAi field through their substantial involvement in companies such as Cephalon Inc., Genta Inc., GlaxoSmithKline plc, Pfizer Inc., Sanofi S.A ("Sanofi"), Sirna Therapeutics, Inc. ("Sirna"), and other companies. Our co-founder and chief executive officer, Douglas M. Fambrough III, Ph.D., was a lead venture capital investor and board member of Sirna, an early RNAi company acquired by Merck & Co., Inc. ("Merck") in 2006 for $1.1 billion.

Corporate Developments

Underwritten Public Offering of Common Stock

On December 18, 2017, we completed an underwritten follow-on public offering of 5,714,286 shares of common stock (the "2017 Offering"). In connection with the 2017 Offering, we entered into an underwriting agreement (the "Underwriting Agreement") with Stifel, Nicolaus & Company, Incorporated and Evercore Group LLC as representatives of the underwriters listed in the Underwriting Agreement (collectively, the "Underwriters"), pursuant to which we granted to the Underwriters a 30-day option to purchase up to an additional 857,143 shares of the Company's common stock (the "Overallotment"). We completed the sale of 6,571,428 shares, including the exercise of the Overallotment, to the Underwriters on December 18, 2017, and that sale resulted in the receipt by the Company of aggregate gross proceeds of $46.0 million, less Underwriter commissions and additional offering expenses totaling approximately $3.2 million.

Redeemable Convertible Preferred Stock

Dicerna no longer has any outstanding shares of redeemable convertible preferred stock. On April 11, 2017, pursuant to a redeemable convertible preferred stock purchase agreement ("SPA") with seven institutional investors (the "Preferred Holders"), led by funds advised by Bain Capital Life Sciences L.P. (the "Lead Investor"), we issued and sold 700,000 shares of our newly designated Redeemable Convertible Preferred Stock, par value $0.0001 per share ("Redeemable Convertible Preferred") to the Preferred Holders in a private placement for aggregate gross proceeds of $70.0 million, less issuance costs of approximately $0.8 million (the "Private Placement"). In addition to the Lead Investor, other participants in the Private Placement included affiliates of Cormorant Asset Management LLC, Domain Associates LLC ("Domain Associates"), EcoR1 Capital LLC, RA Capital Management LLC ("RA Capital") and Skyline Management LLC ("Skyline Ventures"), among others. Domain Associates, RA Capital and Skyline Ventures are entities that are affiliated or were formerly affiliated with certain members of our board of directors.

Per a Certificate of Designation, which was filed with the Secretary of State of the State of Delaware, each holder of Redeemable Convertible Preferred had been entitled to receive cumulative dividends on the Accrued Value, as defined below, of each share of Redeemable Convertible Preferred at an initial rate of 12% per annum, compounded quarterly and subject to two rate reductions, of 4% each, upon the occurrence of certain agreed-upon milestone events. Entering into the BI Agreement constituted a milestone event for purposes of applying the first of two allowable rate reductions to dividends payable on the Redeemable Convertible Preferred. As such, the dividend rate on the Redeemable Convertible Preferred was reduced from 12% to 8% on October 27, 2017. Dividends on the Redeemable Convertible Preferred accrued on the Accrued Value of each share of

Redeemable Convertible Preferred until the conversion thereof, which occurred on December 18, 2017, as discussed below. "Accrued Value" meant, with respect to each share of Redeemable Convertible Preferred, the sum of (i) $100.00 plus (ii) on each quarterly dividend date, an additional amount equal to the dollar value of any dividends on a share of Redeemable Convertible Preferred which had accrued on any dividend payment date and had not previously been added to such Accrued Value.

On March 28, 2017, in accordance with the terms of the SPA, our board of directors voted to increase the size of the board from eight directors to nine directors and approved the appointment of Adam M. Koppel, M.D., Ph.D., a managing director of the Lead Investor, as a director of the Company, effective as of the closing of the Private Placement on April 11, 2017, to fill the resulting vacancy. Dr. Koppel was reelected to the Company's board of directors by shareholder vote in June 2017. We also entered into a registration rights agreement, by and among us and the Preferred Holders (the "Registration Rights Agreement"), pursuant to which the Preferred Holders are entitled to certain demand, shelf and "piggyback" registration rights with respect to the shares of common stock issuable upon conversion of the Redeemable Convertible Preferred, subject to the limitations set forth in the Registration Rights Agreement. The shares of Redeemable Convertible Preferred and the shares of common stock issuable upon conversion of the Redeemable Convertible Preferred were offered and sold by us pursuant to an exemption from the registration requirements of the Securities Act provided by Section 4(a)(2) thereunder.

In connection with the 2017 Offering, we entered into a letter agreement (the "Letter Agreement") with the holders of all of the outstanding shares of our Redeemable Convertible Preferred. Pursuant to the Letter Agreement, the Preferred Holders agreed, subject to the completion of the 2017 Offering, to optionally convert all of their shares of Redeemable Convertible Preferred into common stock. The Letter Agreement also provided for Preferred Holders to waive and amend certain provisions of the Registration Rights Agreement. In consideration for the Preferred Holders agreeing to the optional conversion of the Redeemable Convertible Preferred and to a waiver under and certain amendments to the Registration Rights Agreement, the Company agreed to issue to the Preferred Holders shares of the Company's common stock. Under the Letter Agreement, the number of shares allocable to each Preferred Holder equaled the number of shares of common stock into which the additional dividend accruals on the Redeemable Convertible Preferred that such Preferred Holders would have been entitled to receive up to and including March 31, 2018 are convertible, calculated immediately prior to the effectiveness of the conversion (the "Additional Investor Shares"). The formula for the Additional Investor Shares assumed (1) a conversion price of $3.19 per share of common stock; (2) application of a dividend rate of 12% per annum from April 11, 2017 to October 27, 2017 and (3) application of a dividend rate of 8% per annum commencing from October 28, 2017 through March 31, 2018. March 31, 2018 is approximately the date at which the Company expected to be able to force conversion of the Redeemable Convertible Preferred into shares of common stock, pursuant to the terms of the SPA. On December 18, 2017, we issued an aggregate of 24,206,663 common shares upon full conversion of the Redeemable Convertible Preferred, and no shares of Redeemable Convertible Preferred remain outstanding. In addition to an increase in net loss per share attributable to common shareholders as a result of the recording of deemed and actual dividends, the ultimate impact of the April transaction on the Company's consolidated balance sheet and capital structure, excluding the impact of share issuance costs, was the receipt of $70 million of gross cash proceeds and the issuance of 24,206,663 common shares, or $2.89 per share. This compares to a closing per share price of the Company's common stock of $2.68 on March 28, 2017, the date of signing of the SPA.

On December 29, 2017, we filed with the Secretary of State of the State of Delaware a Certificate of Elimination of the Redeemable Convertible Preferred, which eliminates from our Certificate of Incorporation all matters set forth in the Certificate of Designation of Redeemable Convertible Preferred Stock previously filed with the Secretary of State of the State of Delaware, which established and designated the Redeemable Convertible Preferred Stock and the rights, powers, preferences, privileges and limitations thereof.

Our GalXC RNAi Technology Platform

The RNAi Therapeutic Modality

All of our GalXC drug discovery and development efforts are based on the therapeutic modality of RNAi, a highly potent and specific mechanism for silencing the activity of a targeted gene. In this naturally occurring biological process, double-stranded RNA molecules induce the enzymatic destruction of the mRNA of a target gene that contains sequences that are complementary to one strand of the therapeutic double-stranded RNA molecule. Our 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.

RNAi therapeutics represent a novel advance in drug development. Historically, the pharmaceutical industry has developed small molecules or antibodies to inhibit the activity of disease-causing proteins. This approach is effective for many diseases; nevertheless, many proteins cannot be inhibited by either small molecules or antibodies. Some proteins lack the binding pockets small molecules require for interaction. Other proteins are solely intracellular and therefore inaccessible to antibody-based therapeutics, which are limited to cell surface and extracellular proteins. The novel advantage of RNAi is that instead of targeting proteins, RNAi goes upstream to silence the genes themselves, via the targeted destruction of the mRNAs made from the gene. Rather than seeking to inhibit a protein directly, the RNAi approach is to prevent its creation in the first place.

We believe our approach to RNAi drug development provides the following qualities and advantages compared to other methods of inducing RNAi.

- **We initiate RNAi through the Dicer enzyme**. Our GalXC molecules are structured to be processed by the enzyme Dicer, the initiation point for RNAi in the human cell cytoplasm. Unlike earlier generation RNAi molecules, which mimic the output product of Dicer processing, all our DsiRNAs, including GalXC molecules, enter the RNAi pathway prior to Dicer processing. This can result in preferential use of the correct strand of a double-stranded RNA molecule, and therefore increase the efficacy of the RNAi mechanism. We have found in animal tests that this benefit both increases the potency of our GalXC molecules relative to other RNAi-inducing molecules and enables more sequences to be used compared to other RNAi-inducing molecules. In addition, all our DsiRNAs, including GalXC molecules, have an extended structure relative to conventional RNAi inducing molecules. This extended region presents multiple sites for chemical modification and conjugation compared to earlier RNAi technologies. At these sites, we can use modifications that enhance the drug-like properties on our molecules. Specifically, we can employ modifications that enhance the pharmacokinetic profile and/or suppress immunostimulatory activity.
- **Our GalXC RNAi platform enables subcutaneous dosing for delivery to the liver.** The GalXC RNAi platform is designed to enable convenient subcutaneous delivery for our emerging pipeline of liver-targeted RNAi investigational therapies. The GalXC RNAi platform does not involve LNPs or other formulation components that facilitate drug delivery, which simplifies the platform and eliminates any requirement for functional excipients. Instead, our GalXC molecules are stabilized by chemical modifications and utilize a four base sequence known as a tetraloop, where each base is conjugated to a simple sugar, N-acetylgalactosamine ("GalNAc"), that is specifically recognized by a receptor on the surface of hepatocyte liver cells. With the GalXC RNAi platform, we believe that a full human dose may be administered via a single subcutaneous injection. After injection, the GalXC molecules enter the bloodstream and are exposed to the liver hepatocytes expressing the GalNAc receptor. After binding to the receptor, the GalXC molecules are internalized by the hepatocyte, ultimately enabling the GalXC molecules to access the RNAi machinery inside the hepatocyte. To date, we have demonstrated *in vivo* gene silencing activity with GalXC molecules after subcutaneous administration against nearly three dozen disease-associated genes in the liver.

Optimization of our GalXC molecules

For therapeutic use in humans, our GalXC molecules are optimized both with respect to base sequence and chemical modifications to increase stability and mask them from mechanisms that recognize foreign RNAs, in order to avoid inducing immune system stimulation. Our optimization process begins with an analysis of the target gene sequence using our proprietary GalXC prediction algorithm, which we have developed based on the results of testing thousands of sequences for RNAi activity. We select the sequences with the highest predicted RNAi activity and apply patterns of chemical modification, including a GalNAc-linked tetraloop stem-loop structure, which design-in enhanced stability and hepatocyte delivery specificity and engineers-out immunostimulatory activity. Our GalXC molecules routinely achieve high potencies, with EC50 values in the liver (i.e. the amount of material required to silence a target gene by 50 percent) typically in the 0.1 to 1.0 milligram per kilogram bodyweight (mg/kg) range in *in vivo* studies in mice. We have routinely generated GalXC molecules of this potency within 30 days of doing the initial algorithmic gene sequence analysis, which allows us to explore a large number of potential target genes when selecting our programs.

Our Product Candidates

In choosing clinical programs to pursue using our GalXC technology, we apply the criteria listed below. We believe that our current development programs meet most or all of these criteria.

- **Strength of therapeutic hypothesis.** Our current product candidate gene targets, and those we intend to pursue in the future, are a well-understood part of the disease process where a therapeutic intervention is likely to have substantial benefit for the patient.
- **Readily-identified patient population.** We seek disease indications where patients can be readily identified by the presence of characteristic genetic mutations or other readily-accessible disease features. In the case of genetic diseases, these are heritable genetic mutations that can be identified with available genetic tests.
- **Predictivity of biomarkers for early efficacy assessment.** We seek disease indications where there is a clear relationship between the disease status and an associated biomarker that we can readily measure. This approach will allow us to determine in early stages of clinical development whether our GalXC molecules are likely to have the expected biological and clinical effects in patients.
- **Unmet medical need.** We seek to provide patients with significant benefit and alleviation of disease. The indications we choose to approach have high unmet medical need, which is intended to enable us to better access patients and qualify for pricing and reimbursement that justify our development efforts.
- **Competitive positioning.** We seek indications where we believe we have the opportunity to develop either a first-in-class product or a clearly differentiated therapy.
- **Rapid development path to approval.** To reach commercialization expeditiously and to help ensure our ability to finance development of our product candidates, we have identified indications with the potential for rapid development through marketing approval. Specifically, we believe that some of our product candidates have the potential to obtain breakthrough therapy designation as well as accelerated review process from the FDA.

DCR-PHXC for PH

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

PH encompasses three genetically distinct, autosomal-recessive, inborn errors of glyoxylate metabolism characterized by the over-production of oxalate, a highly insoluble metabolic end-product that is eliminated

mainly by the kidney. Patients with PH are predisposed to the development of multiple and recurrent urinary tract (urolithiasis) and kidney (nephrolithiasis) stones. Calculi formation is accompanied by nephrocalcinosis in some patients with PH (PH1 and some patients with PH2). This deposition of calcium oxalate in the renal parenchyma produces tubular toxicity and renal damage that is compounded by the effects of renal calculi related obstruction and frequent superimposed infections. Based on evaluation of genome sequence databases, there may be as many as 16,000 people with PH in the US and major European countries.

PH1, PH2 and PH type 3 ("PH3"), are each characterized by a specific enzyme deficiency. PH1 is characterized by a deficiency of the liver peroxisomal enzyme alanine: glyoxylate-aminotransferase. Patients with PH1 represent approximately 80% of all patients currently diagnosed with PH. PH2 and PH3 are caused by dysfunction of glyoxylate reductase/hydroxypyruvate reductase and 4-hydroxy-2-oxoglutarate aldolase, respectively. Most patients are diagnosed in childhood or early adulthood. At present, no therapies are approved by regulatory authorities for the treatment of patients with PH. A number of supportive therapies are used in an attempt to mitigate some of the effects of the disease. Current medical management before renal failure develops is underpinned by hyperhydration with fluid intake recommendations of at least 3 liters per day per square meter of body-surface area (5 L/day for a 70-kg adult). These regimens can be problematic in infants and toddlers, necessitating placement of a gastrostomy tube to ensure adequate night time fluid administration. Affected patients are at considerable risk of serious complications during periods of increased fluid loss (fever, diarrhea/vomiting, and urinary tract infections) or when oral hydration is compromised (following surgical procedures). Oral potassium citrate administration is used to inhibit crystallization and alkalinize the urine. In PH1, an approximately 30% or greater reduction in urinary oxalate excretion may be achieved with oral vitamin B6 (Pyridoxine) administration at doses from 5 to 20 mg/kg in a small proportion of affected patients (10-20% of all PH1 patients).

For patients with more advanced disease, dialysis may be used in an attempt to remove endogenously over-produced oxalate. In contrast to 3 times weekly hemodialysis regimens more typically used in other types of renal failure, patients with PH may require hemodialysis 6 or 7 days per week. Given the limitations of dialysis and the inability to impact oxalate over-production substantially in most patients with PH1, most centers now consider liver transplantation approaches earlier in the disease course to minimize the risk of irreversible tissue damage. Current treatments include renal transplantation or, in PH1, combined liver and kidney transplantation. As with organ transplantation in other disease, these procedures are associated with significant medical risk and a requirement for long-term treatment with immunosuppressive drugs that are also associated with significant side effects.

We believe that there is a strong rationale for focusing our RNAi technology on the development of product candidates for the treatment of PH. On July 15, 2017, in a series of presentations at the 12th International Workshop, we presented new preclinical data suggesting the potential utility of DCR-PHXC for treating all forms of PH. In particular, we presented research from animal models demonstrating how DCR-PHXC inhibits the *LDHA* gene, which we have identified as potentially being an optimal therapeutic target in patients with PH. *LDHA* inhibition was shown in animal models to reduce oxalate to normal or near-normal levels in PH1, PH2 and ethylene glycol-induced hyperoxaluria (a model for idiopathic PH).

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

On October 16, 2017, we announced that we had submitted a CTA for DCR-PHXC to the MHRA in the UK. On December 7, 2017, we announced that we dosed the first human in our Phase 1 trial for DCR-PHXC, called PHYOX. We plan to dose the first patient with PH in PHYOX in the second quarter of 2018 and expect to have clinical proof-of-concept data in the second half of 2018. We have submitted CTAs in Germany, France and the Netherlands. Additionally, we expect to initiate a multi-dose Phase 2/3 study in the first quarter of 2019, pending positive POC data and regulatory approval.

Chronic Hepatitis B Virus infection

We are currently using our GalXC RNAi platform to investigate potential pharmaceutical treatments that target HBV. Current therapies for HBV rarely lead to a long-term immunological cure as measured by the clearance of HBsAg and sustained HBV DNA suppression in patient plasma or blood. We have declared a GalXC RNAi platform-based product candidate, DCR-HBVS, and are conducting formal non-clinical development studies. We expect to file an IND and/or a CTA during the fourth quarter of 2018. DCR-HBVS targets HBV messenger RNA. Based on preclinical studies, and only if we receive appropriate regulatory approval to begin human clinical trials, we hope to determine the potential of DCR-HBVS to reduce HBsAg expression and HBV DNA in HBV patients in a subcutaneous dosing paradigm.

According to the Hepatitis B Foundation, globally, HBV is reported to be the most common serious liver infection with over 250 million patients chronically infected, according to an estimate by the World Health Organization. Annual mortality directly linked to chronic HBV infection is estimated to be approximately 780,000 people with an estimated 650,000 of these deaths caused by cirrhosis and liver cancer as a result of chronic hepatitis B, and a further 130,000 of these deaths from complications associated with acute disease. Chronic HBV is characterized by the presence of the HBsAg for six months or more.

Nucleoside analogs and pegylated interferon regimens have been utilized to suppress the virus; however, while the regimens can offer long-term viral suppression if taken continuously, they do not provide a cure. The vast majority of treated patients do not achieve an immunological cure of chronic HBV infection under treatment with these agents. The chance of achieving a long-term immunological cure as measured by the clearance of HBsAg and sustained HBV DNA suppression may be possible with the introduction of novel drugs designed to reduce intrahepatic and serum HBsAg, as well as HBV DNA.

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. The disease is a genetic disorder, where mutations in the disease gene lead to the production of an abnormal protein. The protein causes progressive liver damage and fibrosis, in some cases leading to cirrhosis and liver failure, and we believe that silencing of the disease gene will prevent production of the abnormal protein and thereby slow or stop progression of the liver fibrosis. Greater than 100,000 people in the U.S. are believed to be homozygous for the mutation that causes the liver disease, and at least 10% of those people, and potentially a significantly higher fraction, are believed to have liver-associated disease as a consequence. We plan to seek a risk-sharing collaborator for the program before we file an IND application and/or CTA for this program, which we expect to be prepared to file in the second quarter of 2018.

Hypercholesterolemia

We are using our GalXC RNAi platform to develop a therapeutic that targets the PCSK9 gene for the treatment of hypercholesterolemia. Dicerna has selected a provisional clinical candidate for the program, but is continuing to explore ways to further optimize the program. PCSK9 is a validated target for hypercholesterolemia, and there are FDA-approved therapies targeting PCSK9 that are based on MAb technology. Based on preclinical studies, we believe that our GalXC RNAi platform can produce a PCSK9-targeted therapy with more attractive commercial and treatment 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.

Hypercholesterolemia is characterized by abnormally high blood serum levels of low-density lipoproteins (“LDL”) and is one of the key known risk factors for atherosclerosis and cardiovascular disease (“CVD”).

Managing hypercholesterolemia by lowering LDL is one of the cornerstones of the strategy to reduce the risk of CVD morbidity and mortality.

The use of statins to lower LDL and reduce CVD morbidity and mortality has been successful, although many patients may benefit from additional and alternative therapeutics that more aggressively lower LDL. It is estimated that 35 million U.S. patients are treated with statin therapy with approximately 12 million of these patients classified as suffering from CVD placing them at higher risk of CVD morbidity and mortality. Roughly 37%, or 4.5 million, of these higher risk CVD patients, are not treated to their LDL goal with standard of care therapy: diet and statin drugs. Inhibition of the circulating protein PCSK9 using anti-PCSK9 MAb's has been a strategy utilized to more aggressively lower serum LDL levels than with statin therapy alone.

Additional pipeline programs

In addition to the programs discussed above, we have applied our GalXC technology to multiple gene targets across our disease focus areas of rare diseases, chronic liver diseases and cardiovascular diseases. Pursuant to our strategy, we are seeking collaborations with larger pharmaceutical companies to advance our programs in the areas of chronic liver diseases and cardiovascular diseases. Both these disease areas represent large and diverse patient populations, requiring complex clinical development and commercialization paths that we believe can be more effectively be pursued in collaboration with larger pharmaceutical companies more experienced in these types of programs. The BI Agreement is an example of such a collaboration. For our additional rare diseases, we are continuing to assess their potential for clinical success and market opportunity while optimizing our GalXC molecules.

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

Intellectual Property

We invest significant amounts in research and development. Our research and development expenses were approximately $37.0 million, $41.7 million and $44.0 million in 2017, 2016 and 2015, respectively.

We are seeking multifaceted protection for our intellectual property that includes licenses, confidentiality and non-disclosure agreements, copyrights, patents, trademarks and common law rights, such as trade secrets. We enter into confidentiality and proprietary rights agreements with our employees, consultants, collaborators, subcontractors and other third parties and generally control access to our documentation and proprietary information.

Patents and proprietary rights

We own U.S. patents and a number of pending patent applications with claims to methods and compositions of matter that cover various aspects of our RNAi technology and our discovery technologies, including our proprietary GalXC technology. These U.S. patents include: U.S. 8,349,809 (issued in January 2013, with a projected expiration date of January 2030); U.S. 8,513,207 (issued in August 2013, with a projected expiration date of May 2030); and U.S. 8,927,705 (issued in January 2015, with a projected expiration date of July 2030). We also own numerous patents and patent applications covering specific RNAi sequences that drive activity against high value disease targets, including: KRAS (U.S. 8,372,816; issued in February 2013, with projected expiration in April 2030); HAO1 (U.S. 9,828,606; issued November 2017, with projected expiration in December 2034); CTNNB1 (ß-catenin; U.S. 9,428,752, issued in August 2016, with projected expiration in July 2031); and Alpha-1-antitrypsin (U.S. 9,458,457, issued October 4, 2016, with projected expiration in July 2034). Further, we own various applications and patents with claims to methods and compositions of matter related to

our lipid delivery technology, such as lipid compositions (e.g., U.S. 9,549,983 directed to specific lipid compositions, issued in January 2017, with projected expiration in October 2032) and particle formulations. We have issued or pending claims to RNAi molecules, pharmaceutical compositions/formulations, methods of use, including *in vitro* and *in vivo* methods of reducing target gene expression, methods of treatment, methods of inhibiting cell growth and methods of synthesis.

We jointly own with KHK U.S. and foreign patent applications pursuant to our research collaboration and license agreement claiming developments made in the course of the collaboration focused on delivery of KRAS-specific DsiRNA molecules, including the EnCore formulation process. Depending on the subject matter of future issued claims, we may also jointly own future patents issuing from patent applications filed under the research collaboration and license agreement with KHK.

Our strategy around protection of our proprietary technology, including any innovations and improvements, is to obtain patent coverage in various jurisdictions around the world with a focus on jurisdictions that represent significant global pharmaceutical markets. Generally, patents have a term of 20 years from the earliest non-provisional priority date, assuming that all maintenance fees are paid, no portion of the patent has been terminally disclaimed and the patent has not been invalidated. In certain jurisdictions, and in certain circumstances, patent terms can be extended or shortened. We are obtaining worldwide patent protection for at least novel molecules, composition of matter, pharmaceutical formulations, methods of use, including treatment of disease, methods of manufacture and other novel uses for the inventive molecules originating from our research and development efforts. We continuously assess whether it is strategically more favorable to maintain confidentiality for the "know-how" regarding a novel invention rather than pursue patent protection. For each patent application that is filed we strategically tailor our claims in accordance with the existing patent landscape around a particular technology.

We cannot predict with any certainty if any third-party U.S. or foreign patent rights, other proprietary rights, will be deemed infringed by the use of our technology. Nor can we predict with certainty which, if any, of these rights will or may be asserted against us by third parties. Should we need to defend ourselves and our collaborators against any such claims, substantial costs may be incurred. Furthermore, parties making such claims may be able to obtain injunctive or other equitable relief, which could effectively block our ability to develop or commercialize some or all of our products in the U.S. and abroad, and could result in the award of substantial damages. In the event of a claim of infringement, we or our collaborators may be required to obtain one or more licenses from a third party. There can be no assurance that we can obtain a license on a reasonable basis should we deem it necessary to obtain rights to an alternative technology that meets our needs. The failure to obtain a license may have a material adverse effect on our business, results of operations and financial condition.

We also rely on trade secret protection for our confidential and proprietary information. No assurance can be given that we can meaningfully protect our trade secrets on a continuing basis. Others may independently develop substantially equivalent confidential and proprietary information or otherwise gain access to our trade secrets.

See Item 1A— "Risk Factors — Risks Related to Intellectual Property" for a more detailed discussion of the risks to our intellectual property.

It is our policy to require our employees and consultants, outside scientific collaborators, sponsored researchers and other advisors who receive confidential information from us, to execute confidentiality agreements upon the commencement of employment or consulting relationships. These agreements provide that all confidential information developed or made known to these individuals during the course of the individual's relationship with us is to be kept confidential and is not to be disclosed to third parties except in specific circumstances. The agreements provide that all inventions conceived by an employee shall be our property. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information.

Our success will depend in part on our ability to obtain and maintain patent protection, preserve trade secrets, prevent third parties from infringing upon our proprietary rights and operate without infringing upon the proprietary rights of others, both in the U.S. and other territories worldwide.

Strategic Collaborations

BI collaborative research and license agreement

On October 27, 2017, we entered into the BI Agreement, pursuant to which Dicerna and BI have agreed to jointly research and develop product candidates for the treatment of chronic liver disease, with an initial focus on NASH, using the GalXC platform, our proprietary RNAi-based technology. NASH is caused by the buildup of fat in the liver, potentially leading to liver fibrosis and cirrhosis. It has an especially high prevalence among obese and diabetic patients and is an area of high unmet medical need. The BI Agreement is for the development of product candidates against one target gene with an option for BI to add the development of product candidates that target a second gene. Also pursuant to the BI Agreement, we granted BI a worldwide license in connection with the research and development of the product candidates and will transfer to BI intellectual property rights of the product candidates selected by BI for clinical development and commercialization. We also may provide assistance to BI in order to help BI further develop selected product candidates. Pursuant to the BI Agreement, BI agreed to pay us a non-refundable upfront payment of $10.0 million for the first target. During the term of the research program, BI will reimburse Dicerna the cost of materials and third-party expenses that have been included in the preclinical studies up to an agreed-upon limit. We are eligible to receive up to $191.0 million in potential development and commercial milestones related to the initial target. We are also eligible to receive royalty payments on potential global net sales, subject to certain adjustments, tiered from high single digits up to low double-digits. BI's option to add a second target would provide for an option fee payment and success-based development and commercialization milestones and royalty payments to us.

Through December 31, 2017, we have recognized $1.2 million in revenue associated with the BI Agreement.

KHK research collaboration and license agreement

In December 2009, we entered into a research collaboration and license agreement with KHK for the research, development and commercialization of drug delivery platforms and DsiRNA molecules for therapeutic targets, primarily in oncology (the "KHK Collaboration Agreement"). Under the KHK Collaboration Agreement, we engaged in the discovery of DsiRNA molecules against KRAS and other gene targets nominated by KHK. Since the initiation of the KHK Collaboration 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. We have granted KHK an exclusive license to certain of our technology and patents relating to compounds resulting from the collaboration. KHK has granted us certain non-exclusive licenses in its technology as necessary for us to perform research and development activities as part of the research collaboration.

In November 2017, KHK provided us with notice of termination related to the non-KRAS program. Given our current development focus, including the GalXC program, we no longer consider this agreement material to our business.

License Agreements

City of Hope license agreement

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, royalty-bearing,

worldwide license under certain patent rights in relation to DsiRNA. Under the license agreement, we are obligated to use commercially reasonable efforts to develop and commercialize the licensed products in certain major markets.

The license agreement will remain in effect pursuant to its terms until all of the obligations under the license agreement with respect to the payment of milestones or royalties related to licensed products have terminated or expired. Either party may terminate the license agreement for any uncured material breach by the other party. COH may terminate the license agreement upon our bankruptcy or insolvency. We may terminate the license agreement without cause upon written notice to COH. The COH license applies to our collaboration with KHK. In 2017, we have elected not to make any further diligence extension payments. At this time, however, the license agreement remains in effect and discussions as to next steps are underway. Given our current development focus, including the GalXC program, we no longer consider this agreement material to our business.

Other Licenses

In December 2014, we licensed all of our non-U.S. intellectual property rights to a non-U.S. wholly owned subsidiary. In December 2015, we licensed our U.S. intellectual property rights to the same non-U.S. wholly owned subsidiary. In December 2016, the same non-U.S. wholly owned subsidiary distributed the U.S. intellectual property rights back to us. In 2017, we amended a licensing agreement with the non-U.S. subsidiary to exclude from the scope and operation of that agreement the intellectual property licensed to BI pursuant to the BI Agreement. As such, effective October 27, 2017 certain rights associated with the BI Agreement reverted to us.

Manufacturing and Supply

We do not currently own or operate any manufacturing facilities for the production of preclinical, clinical or commercial quantities of any of our product candidates. For each product candidate, we currently contract with manufacturers, and we expect to continue to do so to meet the preclinical and clinical requirements of our product candidates. We have entered into supply agreements with third parties for supply of certain products and services.

Currently, some of our drug starting materials for our manufacturing activities are supplied by a single source supplier. We have agreements for the supply of such drug materials with manufacturers or suppliers that we believe have sufficient capacity to meet our demands. In addition, we believe that adequate alternative sources for such supplies exist. However, there is a risk that, if supplies are interrupted, it would materially harm our business. We typically order raw materials and services on a purchase order basis and do not enter into long-term dedicated capacity or minimum supply arrangements.

Manufacturing is subject to extensive regulations that impose various procedural and documentation requirements, which govern record keeping, manufacturing processes and controls, personnel, quality control and quality assurance, among others. Our contract manufacturing organizations manufacture our product candidates under current Good Manufacturing Practice (“cGMP”) conditions. cGMP is a regulatory standard for the production of pharmaceuticals that will be used in humans.

Competition

We believe that our scientific knowledge and expertise in RNAi-based therapies provide us with competitive advantages over the various companies and other entities that are attempting to develop similar treatments. However, we face competition at the technology platform and therapeutic indication levels from both large and small biopharmaceutical companies, academic institutions, governmental agencies and public and private research institutions. Many of our competitors have significantly greater financial resources and expertise

in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our success will be based in part upon our ability to identify, develop and manage a portfolio of drugs that are safer and more effective than competing products in the treatment of our targeted patients. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, are more convenient or are less expensive than any products we may develop.

RNA-based therapeutics

To our knowledge, there are no other companies developing GalXC molecules for therapeutic use. However, there are several companies that are currently developing RNAi-based therapies for various indications. We believe that Arrowhead Pharmaceuticals, Inc. ("Arrowhead"), Alnylam and Arbutus Biopharma Corporation ("Arbutus") through their company-specific development or through various collaborations are developing RNAi-based therapies that are competing against our current programs or potential future programs.

Among these, Alnylam, in collaboration with Sanofi Genzyme (a division of Sanofi), is developing multiple genetic rare disease programs including its patisiran ("ALN-TTR") program, which is an RNAi-based therapy for the treatment of hereditary transthyretin-mediated amyloidosis with polyneuropathy ("hATTR-PN") and has completed Phase 3 trials. Alnylam announced the APOLLO study completed enrollment of 225 patients at 44 sites in 19 countries, between December 2013 and January 2016. In early November 2017, Alnylam and Sanofi Genzyme announced positive complete results from the APOLLO Phase 3 study of patisiran. On December 12, 2017, Alnylam announced it had completed submission of an NDA to the U.S. FDA for patisiran for the treatment of adults with hATTR amyloidosis and on December 18, 2017, Alnylam announced it had submitted a Marketing Authorization Application to the European Medicines Agency ("EMA") for the same indication. Pending regulatory approvals, Alnylam will commercialize patisiran in the U.S., Canada and Western Europe, with Genzyme commercializing the product in the rest of the world. In November 2017, Alnylam announced positive preliminary data from a Phase 1/2 study of lumasiran (formerly known as ALN-GO1) in patients with PH. Additional genetic rare disease programs are being developed by Alnylam in collaboration with Sanofi Genzyme including ALN-TTRsc02 for all forms of ATTR amyloidosis; fitusiran ("ALN-AT3"), for the treatment of hemophilia and rare bleeding disorders; ALN-CC5 for the treatment of complement-mediated diseases; and ALN-AS1, for the treatment of acute hepatic porphyrias among others. In addition, Alnylam initiated a Phase 1/2 clinical trial with ALN-HBV for the treatment of HBV infection in mid-2016. In October 2017, Alnylam announced a collaboration with Vir Biotechnology, Inc. ("Vir") for the development and commercialization of RNAi therapeutics for infectious diseases, including chronic HBV infection. The company also announced plans to discontinue further development of ALN-HBV and to advance a new product candidate ALN-HBV02, using the company's ESC+ GalNAc conjugate technology. The Medicines Company ("MDCO") and its collaborator, Alnylam, are advancing an experimental PCSK9 RNAi therapy, inclisiran (formerly known as PCSK9si), for the treatment of hypercholesterolemia. In March 2017, Alnylam and MDCO announced positive final data from the ORION-1 Phase 2 study of inclisiran. The detailed data from ORION-1 showed that inclisiran delivered significant and sustained reductions of LDL-C and high standards of safety and tolerability. In November 2017, Alnylam and MDCO announced the initiation of the Phase 3 clinical program of inclisiran in patients with atherosclerotic cardiovascular disease ("ASCVD").

Arbutus is a clinical-stage biopharmaceutical company developing RNAi-therapeutics for the treatment of chronic HBV infection. Arbutus has multiple HBV programs in development. ARB-1467 is in a multi-dose Phase 2 study in chronic HBV patients, which was initiated in December 2015. Arbutus reported results from this trial based on multiple dose administration of ARB-1467 in Cohorts 1, 2 and 3. The data demonstrated significant

reductions in serum HBsAg levels and showed a step-wise, additive reduction in serum HBsAg with each subsequent dose. Arbutus also presented positive topline results for Cohort 4 (bi-weekly dosing). Overall treatment was well tolerated in all four cohorts. Arbutus has announced that new studies will utilize bi-weekly dosing in a combination study of ARB-1467, with current standard of care nucleot(s)ide analog and interferon therapies, to evaluate the opportunity to improve current cure rates with a finite dosing period. This study is ongoing. Arbutus also reported positive top-line results from a multi-dose healthy volunteer study of AB-423, Arbutus's core protein/capsid formation inhibitor program. The findings showed AB-423 was generally well-tolerated with no serious adverse events. Arbutus has stated that it expects to start a multi-dose study in HBV patients in the first quarter of 2018. AB-506, Arbutus' next-generation capsid inhibitor program, is currently undergoing IND-enabling studies. Pending successful IND-enabling studies, this product candidate could be the subject of an IND (or equivalent) filing. Arbutus has rights under Alnylam's intellectual property to develop RNAi therapeutic products.

Arrowhead is developing RNAi therapeutics and has multiple programs in preclinical development. Arrowhead's most advanced programs include ARO-AAT to treat liver diseases associated with alpha-1 antitrypsin deficiency, and ARO-HBV for chronic HBV. In December 2017, Arrowhead filed regulatory submissions to begin human clinical trials for ARO-AAT and ARO-HBV in New Zealand. Arrowhead's other preclinical programs include: ARO-APOC3 for hypertriglyceridemia; ARO-ANG3 for hypertriglyceridemia; ARO-Lung1 for an undisclosed disease of the lung; ARO-F12 for factor 12 mediated diseases, such as hereditary angioedema and thromboembolic disorders; ARO-HIF2, for the treatment of clear cell renal cell carcinoma associated with HIF-2α; ARO-LPA targeting a polipoprotein A for cardiovascular disease; and ARO-AMG1 for an undisclosed genetically validated cardiovascular target.

In addition to RNAi therapies, there are other intracellular technologies focused on silencing the activity of specific genes by targeting mRNAs copied from them. Companies such as miRagen Therapeutics, Inc., Regulus Therapeutics Inc. and Santaris Pharma A/S, which was acquired by F. Hoffmann-La Roche AG in 2014 and is now known as Roche Innovation Center Copenhagen, target or inhibit or replace microRNAs, which are approximately 22 nucleotides in length, short, non-coding RNAs, to alter mRNA expression levels.

Ionis Pharmaceuticals, Inc. ("Ionis") is discovering and developing RNA-targeted therapeutics based on its antisense technology across multiple therapeutic areas, including severe and rare diseases, cardiovascular diseases, and chronic HBV. Ionis's commercial products include KYNAMRO® (mipomersen sodium) injection for homozygous familial hypercholesterolemia ("HoFH") targeting ApoB-100, which is partnered to Kastle Therapeutics, LLC and Spinraza™ (nusinersen), which received FDA approval for the treatment of spinal muscular atrophy in pediatric and adult patients in December 2016. Biogen Inc. is responsible for commercialization of Spinraza. Ionis has a product pipeline with over two dozen drugs in clinical development. Volanesorsen, a drug candidate in Phase 3 development that Ionis is developing and plans to commercialize through its majority-owned subsidiary, Akcea Therapeutics, Inc. ("Akcea") targets Apo-CIII to treat patients with either familial chylomicronemia syndrome or familial partial lipodystrophy. During the third quarter of 2017, Akcea, working closely with Ionis, filed for marketing authorization for volanesorsen in the U.S., EU and Canada. Akcea is preparing to commercialize volanesorsen for both familial chylomicronemia syndrome and familial partial lipodystrophy, if approved. Additional Phase 3 programs include: IONIS-TTRRx, a drug Ionis is developing with GlaxoSmithKline plc to treat patients with TTR amyloidosis, alicaforsen targeting ICAM-1 for the treatment of pouchitis, an inflammatory bowel disease, which is partnered with Atlantic Healthcare plc; and plazomicin, in development to treat severe bacterial infection and partnered with Achaogen, Inc. In addition, Ionis has multiple programs in Phase 2 development for cardiometabolic diseases and HBV infection, a Phase 2 program for NAFLD/metabolic complications and a Phase 1 program in NASH, as well as clinical programs in many other disease areas.

If our lead product candidates are approved for the indications for which we undertake clinical trials, they may compete with therapies that are either in development or currently marketed by our competitors.

Primary Hyperoxaluria

Currently, there are no approved drugs to treat primary hyperoxaluria. The current standard of care for treating PH is a dual-organ transplant, namely a kidney and liver transplant in patients with PH, which is often difficult to perform due to lack of donors and the threat of organ rejection. Other treatments include pyridoxine regimens and intensive dialysis, as well as treatments generally used in kidney stone disorders such as high-volume fluid intake and oral citrate. These other treatments do not halt disease progression. OxThera AB has a competing approach to PH treatment, currently in late stage clinical development, which is not RNAi-based. In January 2016, Alnylam announced its plans to start a Phase 1 clinical trial for lumasiran (formerly known as ALN-GO1), an investigational RNAi therapeutic for the treatment of PH1. Alnylam presented initial Phase 1 clinical data from its NHV portion of the study in the third quarter of 2016 at the IPNA. In November 2017, Alnylam announced positive preliminary data from a Phase 1/2 study of lumasiran in patients with PH. Allena Pharmaceuticals, Inc. has announced its plans to initiate, in the first quarter of 2018, a Phase 2 clinical trial of ALLN-177, a first-in-class, non-absorbed, orally-administered enzyme for the treatment of hyperoxaluria in adolescents and adults with PH or severe forms of secondary hyperoxaluria, with interim data expected in the second half of 2018.

Hypercholesterolemia

Repatha® (evolocumab) was the second PCSK9 MAb inhibitor to receive FDA approval. Developed by Amgen, Inc. ("Amgen"), Repatha was approved in August 2015 for use in addition to diet and maximally-tolerated statin therapy in adults with heterozygous familial hypercholesterolemia, HoFH, or clinical atherosclerotic cardiovascular disease, such as heart attacks or strokes, who require additional lowering of LDL cholesterol.

Praluent® (alirocumab) was approved in July 2015 and launched in the U.S. as a second line treatment for adults with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease whose LDL cholesterol is not adequately controlled by diet and statin treatment. Alirocumab was the first anti-PCSK9 MAb to receive FDA approval and was developed by Sanofi and Regeneron Pharmaceuticals, Inc. ("Regeneron"). In October 2017, Regeneron and Sanofi announced that the U.S. Court of Appeals for the Federal Circuit has ordered a new trial and vacated the permanent injunction in the dispute concerning Amgen's asserted patent claims for antibodies targeting PCSK9 (proprotein convertase subtilisin/kexin type 9). This ruling means that Sanofi and Regeneron will continue marketing, selling and manufacturing Praluent® (alirocumab) injection in the U.S. A Phase 3 study of Praluent® (alirocumab) injection in HoFH was initiated in the fourth quarter of 2017.

There are additional anti-PCSK9 MAb therapies in clinical development. Multiple cardiovascular outcome studies are being conducted with the anti-PCSK9 MAb therapies to determine if these higher risk patients will have superior cardiovascular outcomes vs. patients treated with standard of care. On February 2, 2017, Amgen announced that the FOURIER (Further Cardiovascular Outcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk) trial studying Repatha's ability to reduce cardiovascular risk in atherosclerotic patients met its primary endpoint. On March 17, 2017, at the American College of Cardiology's 66th Annual Scientific Session, Amgen presented positive results showing that Repatha (Evolocumab) decreases LDL-C levels and reduces risk of cardiovascular events.

MDCO and its collaborator, Alnylam, are advancing an experimental PCSK9 RNAi therapy, inclisiran (formerly PCSK9si), which has a similar mechanism of action as Dicerna's GalXC PCSK9 compound. Inclisiran is being studied in a placebo-controlled, double-blind, randomized Phase 2 trial of single or multiple subcutaneous injections in a total of 501 patients with ASCVD or ASCVD-risk equivalents (e.g., diabetes and familial hypercholesterolemia) and elevated LDL-C despite maximum tolerated doses of LDL-C lowering therapies. The primary endpoint of the study, known as ORION-1, is the percentage change in LDL-C levels from baseline at Day 180. Preliminary topline data from the study, presented at the American Heart Association

Scientific Sessions in November 2016, show that inclisiran was generally well tolerated and no material safety issue was observed, including no elevations of liver enzymes considered related to study medication and no neuropathy or change in renal function, and that the study met all interim analysis goals. In March 2017, Alnylam and MDCO announced positive final data from the ORION-1 Phase 2 study of inclisiran. The detailed data from ORION-1 showed that inclisiran delivered significant and sustained reductions of LDL-C and high standards of safety and tolerability. In November 2017, Alnylam and MDCO announced the initiation of the Phase 3 clinical program of inclisiran in patients with atherosclerotic cardiovascular disease ASCVD.

Government Regulation and Product Approval

Governmental authorities in the U.S., at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, promotion, storage, record-keeping, advertising, distribution, sampling, pricing, sales and marketing, safety, post-approval monitoring and reporting, and export and import of products such as those we are developing. Our product candidates must be approved by the FDA through the NDA process before they may be legally marketed in the U.S. and will be subject to similar requirements in other countries prior to marketing in those countries. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources and the extensive laws and regulations that apply to drug products and product candidates in the U.S. are subject to change.

U.S. government regulation

NDA approval processes

In the U.S., the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act (the "FDCA") and implementing regulations. Failure to comply with the applicable U.S. requirements at any time during the product development or approval process, or after approval, may result in a delay of approval or subject an applicant to administrative or judicial sanctions, any of which could have a material adverse effect on us. These sanctions could include:

- refusal to approve pending applications;
- withdrawal of an approval;
- imposition of a clinical hold;
- issuance of warning or untitled letters;
- product recalls;
- product seizures;
- refusals of government contracts;
- total or partial suspension of production or distribution; or
- injunctions, fines, restitution, disgorgement, civil penalties or criminal prosecution.

The process required by the FDA before a drug may be marketed in the U.S. generally includes the following:

- completion of nonclinical laboratory tests, animal studies and formulation studies conducted according to Good Laboratory Practices ("GLPs") or other applicable laws and regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an institutional review board ("IRB") at each clinical site before each trial may be initiated

- performance and inspection of adequate and well-controlled human clinical trials and clinical data according to FDA regulations and Good Clinical Practices ("GCP") to establish the safety and efficacy of the product candidate for its intended use;
- submission of an NDA to the FDA and the FDA's acceptance of the NDA for filing;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product candidate is produced to assess compliance with cGMP to assure that the facilities, methods and controls are adequate to preserve the product candidate's identity, strength, quality and purity;
- satisfactory completion of an FDA inspection of the major investigational sites to ensure data integrity and assess compliance with GCP requirements; and
- FDA review and approval of the NDA.

Once a pharmaceutical candidate is identified for development, it enters the preclinical or nonclinical testing stage. Nonclinical tests include laboratory evaluations of product chemistry, stability, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the nonclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. Some nonclinical testing may continue even after the IND is submitted. In addition to including the results of the nonclinical studies, the IND will also include a protocol detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the first phase lends itself to an efficacy determination. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the IND on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. A clinical hold may occur at any time during the life of an IND and may affect one or more specific studies or all studies conducted under the IND.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with FDA regulations and GCP. They must be conducted under protocols detailing the objectives of the trial, dosing procedures, research subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol and protocol amendments must be submitted to the FDA as part of the IND, and progress reports detailing the status of the clinical trials must be submitted to the FDA annually. Sponsors also must timely report to the FDA serious and unexpected adverse reactions, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigation brochure or any findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug. All research subjects or their legally authorized representatives must provide their informed consent in writing prior to their participation in a clinical trial. An IRB at each institution participating in the clinical trial must review and approve the protocol and the informed consent form before a clinical trial commences at that institution, monitor the study until completed and otherwise comply with IRB regulations. Information about most clinical trials must be submitted within specific timeframes to the National Institutes of Health ("NIH") to be publicly posted on the ClinicalTrials.gov website.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined.

- Phase 1—The product candidate is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and elimination. In the case of some product candidates for severe or life-threatening diseases, such as cancer, especially when the product candidate may be inherently too toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- Phase 2—Clinical trials are performed on a limited patient population intended to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3—Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the product and provide an adequate basis for product labeling.

Human clinical trials are inherently uncertain and Phase 1, Phase 2 and Phase 3 testing may not be successfully completed. The FDA, the sponsor, or a data safety monitoring board, may suspend a clinical trial at any time for a variety of reasons, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

During the development of a new product candidate, sponsors are given opportunities to meet with the FDA at certain points prior to the submission of an IND, at the end of Phase 2 and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date and for the FDA to provide advice on the next phase of development. Sponsors typically use the meeting at the end of Phase 2 to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial that they believe will support the approval of an NDA. If a Phase 2 clinical trial is the subject of discussion at the end of Phase 2 meeting with the FDA, a sponsor may be able to request a Special Protocol Assessment, the purpose of which is to reach agreement with the FDA on the Phase 3 clinical trial protocol design and analysis that will form the primary basis of an efficacy claim.

Concurrent with clinical trials, sponsors usually complete additional animal safety studies and also develop additional information about the chemistry and physical characteristics of the product candidate and finalize a process for manufacturing commercial quantities of the product candidate in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and the manufacturer must develop methods for testing the safety, identity, strength, purity, and quality of the product candidate. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its proposed shelf-life. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured and tested and will not approve the product unless cGMP compliance is satisfactory. The FDA will also typically inspect one or more clinical sites to assure compliance with FDA regulations and GCP.

The results of product development, nonclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests and other control mechanisms, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of user fees, but a waiver of such fees may be obtained under specified circumstances. The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. It may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant. The FDA typically requires that an NDA include data from two adequate and well-controlled clinical trials, but approval may be based upon a single adequate and well-controlled clinical trial in certain circumstances. The FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data. Even if such data are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. The FDA may refer the NDA to an advisory committee for review and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the

product labeling. In addition, the FDA may condition approval on the completion of post approval studies. Such studies may involve clinical trials designed to further assess a product's safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. If the FDA determines that it is necessary to ensure the safe use of the drug, the FDA may also condition approval on the implementation of a risk evaluation and mitigation strategy ("REMS"). The REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

Expedited review and approval

The FDA has various programs, including Fast Track, priority review, breakthrough, and accelerated approval, which are intended to expedite or simplify the process for reviewing product candidates. Generally, product candidates that are eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs and those that offer meaningful benefits over existing treatments. A sponsor can request application of these programs either alone or in combination with each other, depending on the circumstances. Even if a product candidate qualifies for one or more of these programs, the FDA may later decide that the product candidate no longer meets the conditions for qualification or that the time period for FDA review or approval will be shortened. None of the expedited approval programs change the NDA approval standard applied to a product.

New drugs are eligible for Fast Track status if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track status entitles such a drug to expedited review and frequent contact with the FDA review division. Unlike other expedited review programs, Fast Track designation allows the FDA to accept for review individual sections of the NDA on a rolling basis. The FDA may also grant a priority review designation to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months from filing of an NDA, rather than the standard review of ten months from filing under current Prescription Drug User Fee Act guidelines. Most products that are eligible for Fast Track designation are also likely to be considered appropriate to receive a priority review.

Drug products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA typically requires that a sponsor of a product candidate receiving accelerated approval conduct post-approval clinical trials. As an additional condition of approval, the FDA currently requires pre-approval of all promotional materials, which could adversely impact the timing of the commercial launch of the product.

The FDA may expedite the approval of a designated breakthrough therapy, which is a drug that is intended to treat a serious or life-threatening disease or condition for which preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. A sponsor may request that a drug be designated as a breakthrough therapy at any time during the clinical development of the product. If the FDA designates a drug as a breakthrough therapy, the FDA must take actions appropriate to expedite the development and review of the application, which may include holding meetings with the sponsor and the review team throughout the development of the drug; providing timely advice to the sponsor regarding the development of the drug to ensure that the development program is as efficient as practicable; involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review; and taking steps to ensure that the design of the clinical trials is as efficient as practicable.

In December 2016, the 21st Century Cures Act ("Cures Act"), was signed into law. The Cures Act included numerous provisions that may be relevant to our product candidates, including provisions designed to speed development of innovative and breakthrough therapies. The Cures Act amends the FDCA and the Public Health Service Act, to reauthorize and expand funding for the NIH and to authorize the FDA to increase spending on innovation projects. Central to the Cures Act are provisions that enhance and accelerate the FDA's processes for reviewing and approving new drugs and supplements to approved NDAs. The Cures Act also includes a provision that requires certain manufacturers or distributors of an investigational drug to make their policies on the availability of certain expanded access programs publicly available. Because the Cures Act was enacted relatively recently and the FDA may take several years to develop these policies, it is difficult to know whether or how the Cures Act will affect our business.

Patent term restoration and marketing exclusivity

Depending upon the timing, duration and specifics of FDA approval of the use of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product candidate's approval date. The patent term restoration period is generally one half of the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved product candidate is eligible for the extension and the application for extension must be made prior to expiration of the patent. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restorations of patent term for some of our currently owned or licensed patents to add patent life beyond their current expiration date, depending on the expected length of clinical trials and other factors involved in the submission of the relevant NDA.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the U.S. to the first applicant to gain approval of an NDA for a new chemical entity. A product candidate is a new chemical entity if the FDA has not previously approved any other new product candidate containing the same active moiety, which is the molecule or ion responsible for the action of the product candidate substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application ("ANDA") or a 505(b)(2) NDA (i.e., an NDA that contains full safety and effectiveness reports but allows at least some of the information required for NDA approval to come from studies not conducted by or for the applicant) submitted by another company for another version of such product candidate where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an approved NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing product candidate. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for product candidates containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Orphan drug designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to product candidates intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000

individuals in the U.S. or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making available in the U.S. a product candidate for this type of disease or condition will be recovered from sales in the U.S. for that product candidate. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product candidate that has orphan drug designation subsequently receives the first FDA approval for the disease 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 including a full NDA 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 prior to us.

On August 8, 2017, the FDA Reauthorization Act of 2017 ("FDARA") was enacted. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act, including the FDARA amendment, its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Pediatric exclusivity, pediatric use and rare pediatric disease priority review vouchers

Under the Best Pharmaceuticals for Children Act, certain product candidates may obtain an additional six months of exclusivity if the sponsor submits information requested in writing by the FDA (a "Written Request") relating to the use of the active moiety of the product candidate in children. The FDA may not issue a Written Request for studies on unapproved or approved indications or where it determines that information relating to the use of a product candidate in a pediatric population, or part of the pediatric population, may not produce health benefits in that population.

FDARA amended the FDCA to provide that a drug, for which an application has been submitted or approved pursuant to section 505(b)(2) or 505(j) of the FDCA, will not be considered ineligible for approval or misbranded because the labeling of such drug omits a pediatric indication or other pediatric labeling information when the omitted pediatric information is protected by patent or marketing exclusivity. FDARA further permits FDA to require specific labeling for such products related to the omitted pediatric indication and information to, among other things, make clear that the omission of the information is related to the exclusivity. We do not know if or how such changes to the pediatric exclusivity provisions might affect our business.

In addition, the Pediatric Research Equity Act ("PREA") requires a sponsor to conduct pediatric studies for most product candidates and biologics, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs, biologics license applications and supplements thereto must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must assess the safety and effectiveness of the product candidate for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product candidate is safe and effective. The sponsor or the FDA may request a deferral of pediatric studies for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the product candidate or biologic is ready for approval for use in adults before pediatric studies are complete or that additional safety or effectiveness data needs to be collected before the pediatric studies begin. After April 2013, the FDA must send a noncompliance letter to any sponsor that fails to

submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation. PREA does not apply to any drug for an indication for which orphan designation has been granted. However, if only one indication for a product has orphan designation, a pediatric assessment may still be required for any applications to market that same product for the non-orphan indication(s).

Section 529 of the FDCA is intended to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Although there are existing incentive programs to encourage the development and study of drugs for rare diseases, pediatric populations, and unmet medical needs, section 529 provides an additional incentive for rare pediatric diseases, which may be used alone or in combination with other incentive programs. "Rare pediatric disease" is defined as a disease that:

- "primarily affects individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents," which is interpreted as meaning that greater than 50% of the affected population in the U.S. is aged 0 through 18 years; and
- is "a rare disease or condition" as defined in the FDCA, which includes diseases and conditions that affect fewer than 200,000 persons in the U.S. and diseases and conditions that affect a larger number of persons and for which there is no reasonable expectation that the costs of developing and making available the drug in the U.S. can be recovered from sales of the drug in the U.S.

Under section 529, the sponsor of a human drug application for a rare pediatric disease drug product may be eligible for a voucher that can be used (or sold) to obtain a priority review for a subsequent human drug application submitted under section 505(b)(1) of the FDCA or section 351 of the Public Health Service Act after the date of approval of the rare pediatric disease drug product. The rare pediatric disease priority review vouchers program was re-authorized by Congress in the Cures Act, extending the program through 2020. The FDA has issued draft Guidance for Industry for Rare Pediatric Disease Priority Review Vouchers.

Post-approval requirements

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product candidate reaches the market. Requirements for additional Phase 4 trials (post-approval marketing studies) to confirm safety and efficacy may be imposed as a condition of approval. Later discovery of previously unknown problems with a product candidate may result in REMS or even complete withdrawal of the product candidate from the market. After approval, some types of changes to the approved product candidate, such as adding new indications, manufacturing changes and additional labeling changes, are subject to further FDA review and approval. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved product candidates that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product candidate based on the results of these post-marketing programs.

Any product candidates manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things:

- record-keeping requirements;
- reporting of adverse experiences with the product candidate;
- submission of periodic reports;
- providing the FDA with updated safety and efficacy information;
- drug sampling, stability and distribution requirements;
- notifying the FDA and gaining its approval of specified manufacturing or labeling changes; and
- complying with statutory and regulatory requirements for promotion and advertising.

Drug manufacturers and other entities involved in the manufacture and distribution of approved product candidates are required to register their establishments and provide product listing information to the FDA and

certain state agencies and are subject to periodic unannounced inspections by the FDA and some state agencies for compliance with cGMP and other laws.

Regulation outside of the U.S.

In addition to regulations in the U.S., we will be subject to regulations of other jurisdictions governing any clinical trials and commercial sales and distribution of our product candidates. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of countries outside of the U.S. before we can commence clinical trials in such countries, and approval of the regulators of such countries or supranational areas, such as the European Union ("EU"), before we may market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Under EU regulatory systems, a company may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure, which is compulsory for certain medicines, including those produced by biotechnology or those intended to treat HIV, AIDS, cancer, neurodegenerative disorders, autoimmune and other immune dysfunctions, viral diseases or diabetes and is optional for those medicines which are a significant therapeutic, scientific or technical innovation or whose authorization would be in the interest of public health, provides for the grant of a single marketing authorization that is valid for all EU member states. Through the decentralized procedure, a medicinal product that has not yet been authorized in the EU can be simultaneously authorized in several EU member states. The mutual recognition procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization may submit an application to the remaining member states. Within 90 days of receiving the applications and assessment reports, each member state must decide whether to recognize the approval. If a member state does not recognize the marketing authorization, the disputed points are eventually referred to the European Commission, whose decision is binding on all member states.

As in the U.S., we may apply for designation of a product candidate as an orphan drug for the treatment of a specific indication in the EU before the application for marketing authorization is made. Sponsors of orphan drugs in the EU can enjoy economic and marketing benefits, including up to ten years of market exclusivity for the approved indication. During such period, marketing authorization applications for "similar" medicinal products will not be accepted, unless another applicant can show that its product is safer, more effective or otherwise clinically superior to the orphan-designated product. In the EU, a "similar medicinal product" is a medicinal product containing a similar active substance or substances as contained in a currently authorized orphan medicinal product, and which is intended for the same therapeutic indication.

Coverage and Reimbursement

Sales of our products will depend, in part, on the extent to which the costs of our products will be covered and paid for by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. Third-party payors may limit coverage to specific products on an approved list or formulary, which might not include all of the FDA-approved products for a particular indication. Also, third-party payors may refuse to include a particular branded drug on their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or another alternative is available. Third-party payors are increasingly challenging the prices charged for medical products and services. Additionally, the containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. For example, the current U.S. administration has indicated support for possible new measures to regulate drug pricing. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could significantly limit our net revenue and financial results. If these third-party payors

do not consider our products to be cost-effective compared to other therapies, they may not cover our products after approved as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA") imposed new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities which will provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for our products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010, collectively referred to as the ACA, enacted in March 2010, has had a significant impact on the health care industry by, for example, expanding coverage for the uninsured and seeking to contain overall healthcare costs. With regard to pharmaceutical products, among other things, the ACA contains provisions that may reduce the profitability of drug products such as expanding and increasing industry rebates for drugs covered under Medicaid programs and making changes to the coverage requirements under the Medicare Part D program. Recently, the current U.S. administration and U.S. Congress have expressed a desire to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA, which has contributed to the uncertainty of the ongoing implementation and impact of the ACA and also underscores the potential for additional health care reform going forward. For example, the newly enacted federal income tax law includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Congress may consider other legislation that would alter other aspects of the ACA. There is still uncertainty with respect to the impact the current U.S. administration and the U.S. Congress may have, if any, and any changes will likely take time to unfold. 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.

Further legislation or regulation could be passed that could harm our business, financial condition and results of operations. Other legislative changes have been proposed and adopted since the ACA was enacted. For example, in August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction of at least $1.2 trillion for fiscal years 2012 through 2021, triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect beginning on April 1, 2013 and will stay in effect through 2027 unless additional Congressional action is taken. In addition, on February 9, 2018, Congress passed the Bipartisan Budget Act that made a number of healthcare reforms. For example, the law changes the discounts manufacturers are required to apply to their drugs under the Coverage Gap Discount Program from 50% to 70% of the negotiated price starting in 2019. In addition, the law increases civil and criminal penalties for fraud and abuse laws, including, for example, criminal fines for violations of the Anti-Kickback Statute increase from $25,000 to $100,000 and corresponding prison sentences also increase from no more than five years to no more than ten years.

Also, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which have resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. Individual states in the United States have also become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures. For example, in September 2017, the California State Assembly approved SB17 which requires pharmaceutical companies to notify health insurers and government health plans at least 60 days before any scheduled increases in the prices of their products if they exceed 16% over a two-year period, and further requiring pharmaceutical companies to explain the reasons for such increase. Effective in 2016, Vermont passed a law requiring certain manufacturer identified by the state to justify their price increases.

In addition, in some non-U.S. jurisdictions, the proposed pricing for a product candidate must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls and/or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Historically, product candidates launched in the EU do not follow price structures of the U.S. and generally tend to have price structures that are significantly lower.

Other Healthcare Fraud and Laws

In the U.S., our activities are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including but not limited to, the Centers for Medicare and Medicaid Services ("CMS") other divisions of the U.S. Department of Health and Human Services (such as the Office of Inspector General and the Health Resources and Service Administration), the U.S. Department of Justice (the "DOJ") and individual U.S. Attorney offices within the DOJ, and state and local governments. For example, sales, marketing and scientific/educational grant programs may have to comply with the anti-fraud and abuse provisions of the Social Security Act, the false claims laws, the privacy and security provisions of the Health Insurance Portability and Accountability Act ("HIPAA") and similar state laws, each as amended, as applicable.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. The Anti- Kickback Statute has been interpreted to apply to arrangements between therapeutic product manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Additionally, the intent standard under the Anti-Kickback Statute was amended by the ACA to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act (the "FCA") (discussed below).

The federal false claims and civil monetary penalty laws, including the FCA, which imposes significant penalties and can be enforced by private citizens through civil qui tam actions, prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false or fraudulent claim for payment to, or approval by, the federal healthcare programs, including Medicare and Medicaid, or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. For instance, historically, pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, off-label, and thus generally non-reimbursable, uses.

HIPAA created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the Anti-Kickback Statute, the ACA amended the intent standard for certain healthcare fraud statutes under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

Also, many states have similar, and typically more prohibitive, fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Additionally, to the extent that our product candidates may in the future be sold in a foreign country, we may be subject to similar foreign laws.

We may be subject to data privacy and security regulations by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH") and its implementing regulations, imposes requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to business associates, independent contractors, or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, many state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways, are often not pre-empted by HIPAA, and may have a more prohibitive effect than HIPAA, thus complicating compliance efforts.

We expect our product candidates, once approved, may be eligible for coverage under Medicare, the federal health care program that provides health care benefits to the aged and disabled, and covers outpatient services and supplies, including certain pharmaceutical products, that are medically necessary to treat a beneficiary's health condition. In addition, our product candidates may be covered and reimbursed under other government programs, such as Medicaid and the 340B Drug Pricing Program. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Under the 340B Drug Pricing Program, the manufacturer must extend discounts to entities that participate in the program. As part of the requirements to participate in certain government programs, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average manufacturer price, or AMP, and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely.

Additionally, the federal Physician Payments Sunshine Act (the "Sunshine Act"), within the ACA, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report annually to CMS information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members. Failure to report accurately could result in penalties. In addition, many states also govern the reporting of payments or other transfers of value, many of which differ from each other in significant ways, are often not pre-empted, and may have a more prohibitive effect than the Sunshine Act, thus further complicating compliance efforts.

Environment

Our third-party manufacturers are subject to inspections by the FDA for compliance with cGMP and other U.S. regulatory requirements, including U.S. federal, state and local regulations regarding environmental protection and hazardous and controlled substance controls, among others. Environmental laws and regulations are complex, change frequently and have tended to become more stringent over time. We have incurred, and may continue to incur, significant expenditures to ensure we are in compliance with these laws and regulations. We would be subject to significant penalties for failure to comply with these laws and regulations.

Sales and Marketing

Our current focus is on the development of our existing portfolio, the initiation and completion of clinical trials and, if and where appropriate, the registration of our product candidates. We currently do not have marketing, sales and distribution capabilities. If we receive marketing and commercialization approval for any of our product candidates, we intend to market the product either directly or through strategic alliances and distribution agreements with third parties. The ultimate implementation of our strategy for realizing the financial value of our product candidates is dependent on the results of clinical trials for our product candidates, the availability of funds, our ability to obtain adequate coverage and reimbursement of our products, compliance with laws governing our sales and marketing activities, and the ability to negotiate acceptable commercial terms with third parties.

Employees

As of December 31, 2017, we had 44 full-time employees, of whom 32 are engaged in research and development and 12 in administration. None of our employees are represented by a labor union or covered by a collective bargaining agreement. Geographically, 39 of our employees are located in Massachusetts, four in Colorado and one in New Jersey. We consider our relationship with our employees to be good.

Corporate Information

We were incorporated in Delaware in 2006. We maintain our executive offices at 87 Cambridgepark Drive, Cambridge, MA 02140, and our main telephone number is (617) 621-8097. Our website address is *www.dicerna.com*, which contains information about us. The information contained in, or that can be accessed through, our website is not part of, and is not incorporated in the documents we file with the Securities and Exchange Commission ("SEC").

The information in, or that can be accessed through, our website is not part of this Annual Report on Form 10-K. Our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K and amendments to those reports are available, free of charge, on or through our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The public may read and copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C.

20549. Information on the operation of the Public Reference Room can be obtained by calling 1-800-SEC-0330. The SEC maintains an Internet site that contains reports, proxy and information statements and other information regarding our filings at *www.sec.gov*.

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an emerging growth company until the earlier of: (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of our initial public offering on February 4, 2014, (b) in which we have total annual gross revenue of at least $1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of the prior June 30th, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period. We refer to the Jumpstart Our Business Startups Act of 2012 herein as the "JOBS Act," and references herein to "emerging growth company" shall have the meaning associated with it in the JOBS Act.

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

Risks Related to Our Business

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

We will need to raise substantial additional funds to expand our development, regulatory, manufacturing, marketing and sales capabilities, whether internally or through other organizations. We have used substantial funds to develop our product candidates and delivery technologies and will require significant funds to conduct further research and development and preclinical testing and clinical trials of our product candidates, to seek regulatory approvals for our product candidates and to manufacture and market products, if any are approved for commercial sale. As of December 31, 2017, we had $113.7 million in cash and cash equivalents and held-to-maturity investments. Based on our current operating plan and liquidity, including the receipt of $69.3 million in net proceeds in connection with the issuance of the Redeemable Convertible Preferred on April 11, 2017, the receipt of $42.8 million in net proceeds in connection with the 2017 Offering and the receipt of upfront proceeds in connection with the BI Agreement, we believe that our available cash, cash equivalents and held-to-maturity investments will be sufficient to fund our planned level of operations for at least the 12-month period following March 8, 2018. Our future capital requirements and the period for which we expect our existing resources to support our operations may vary significantly from what we expect. Our monthly spending levels vary based on new and ongoing development and corporate activities. Because the length of time and activities associated with successful development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. To execute our business plan, we will need, among other things:

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

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

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

We are a biopharmaceutical company with a limited operating history focused on the discovery and development of treatments based on the emerging therapeutic modality RNAi, a biological process in which RNA molecules inhibit gene expression. Since our inception in October 2006, we have devoted our resources to the development of DsiRNA molecules and delivery technologies. We have had significant operating losses since our inception. As of December 31, 2017, we had an accumulated deficit of $315.8 million. For the years ended December 31, 2017, 2016 and 2015, our net loss attributable to common stockholders was $80.1 million, $59.5 million and $62.8 million, respectively. Substantially all of our operating losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. Our technologies and product candidates are in early stages of development, and we are subject to the risks of failure inherent in the development of product candidates based on novel technologies.

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

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

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

- variations in the level of expense related to our product candidates or future development programs;
- results of clinical trials, or the addition or termination of clinical trials or funding support by us, our existing collaborators or any future collaborator or licensor;
- the timing of the release of results from any clinical trials conducted by us or our collaborator BI;
- our execution of any collaboration, licensing or similar arrangement, and the timing of payments we may make or receive under such existing or future arrangements or the termination or modification of any such existing or future arrangements;
- any intellectual property infringement or misappropriation lawsuit or opposition, interference, re-examination, post-grant review, inter partes review, nullification, derivation action, or cancellation proceeding in which we may become involved, including Alnylam's lawsuit alleging misappropriation of confidential information and trade secrets;
- additions and departures of key personnel;
- strategic decisions by us and our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- if any of our product candidates receive regulatory approval, market acceptance and demand for such product candidates;
- if any of our third-party manufacturers fail to execute on our manufacturing requirements;
- regulatory developments affecting our product candidates or those of our competitors;
- disputes concerning patents, proprietary rights, or license and collaboration agreements that negatively impact our receipt of milestone payments or royalties or require us to make significant payments arising from licenses, settlements, adverse judgments or ongoing royalties; and
- changes in general market and economic conditions.

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

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

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

Relatively few product candidates based on RNAi have been tested in animals or humans, and a number of clinical trials conducted by other companies using RNAi technologies have not been successful. We may

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

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

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

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

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

- our ability to compliantly market and sell our products; and
- availability of alternative effective treatments for the disease indications our product candidates are intended to treat and the relative risks, benefits and costs of those treatments.

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

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

Even if we, or any future collaborators, obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

On August 3, 2017, the Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's preexisting regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

As in the U.S., we may apply for designation of a product candidate as an orphan drug for the treatment of a specific indication in the EU before the application for marketing authorization is made. Sponsors of orphan drugs in the EU can enjoy economic and marketing benefits, including up to ten years of market exclusivity for the approved indication. During such period, marketing authorization applications for a "similar medicinal product" will not be accepted, unless another applicant can show that its product is safer, more effective or otherwise clinically superior to the orphan-designated product. In the EU, a "similar medicinal product" is a medicinal product containing a similar active substance or substances as contained in a currently authorized orphan medicinal product, and which is intended for the same therapeutic indication. The respective orphan designation and exclusivity frameworks in the U.S. and in the EU are subject to change, and any such changes may affect our ability to obtain EU or U.S. orphan designations in the future.

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

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

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

- negative or inconclusive results from our clinical trials or the clinical trials of others for product candidates similar to ours, leading to a decision or requirement to conduct additional preclinical testing or clinical trials or abandon a program;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- delays in submitting 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 EMA, regarding the scope or design of our clinical trials;
- delays in enrolling individuals in clinical trials;
- high drop-out rates of study participants;
- inadequate supply or quality of drug product or product candidate components or materials or other supplies necessary for the conduct of our clinical trials;
- greater than anticipated clinical trial costs;
- poor effectiveness of our product candidates during clinical trials;

- unfavorable FDA or other regulatory agency inspection and review of a clinical trial site;
- failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;
- delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular; and
- varying interpretations of data by the FDA and foreign regulatory agencies.

We are dependent on BI for the successful development of product candidates in the collaboration.

On October 27, 2017, we entered into the BI Agreement to jointly research and develop candidate products using the GalXC platform to target specific disease-linked genes in the hepatocytes for the treatment of NASH. Under the terms of the BI Agreement, BI agreed to pay us a non-refundable upfront payment of $10.0 million, and we will be eligible to receive up to $191.0 million in development and commercial milestones related to the initial target and royalty payments on global net sales. Once a product candidate is selected, the success of our collaboration with BI and the realization of the milestone and royalty payments under the BI Agreement depends entirely upon the efforts of BI, which may not be successful in obtaining approvals for the product candidates developed under the collaboration or in marketing, or arranging for necessary supply, manufacturing or distribution relationships for, any approved products. BI may change its strategic focus or pursue alternative technologies in a manner that results in reduced, delayed or no revenue to us. BI has a variety of marketed products and product candidates under collaboration with other companies, possibly including some of our competitors, and BI's own corporate objectives may not be consistent with our interests. If BI fails to develop, obtain regulatory approval for or ultimately commercialize any product candidate under our collaboration or if BI terminates our collaboration, our business, financial condition, results of operations and prospects could be materially and adversely affected. In addition, if we have a dispute or enter into litigation with BI in the future, it could delay development programs, create uncertainty as to ownership of intellectual property rights, distract management from other business activities and generate substantial expense.

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

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

If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of preclinical studies or clinical trials or meet expected deadlines, our clinical development programs could be delayed and otherwise adversely affected. In all events, we are responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the general investigational plan and protocols for the trial as well as applicable laws and regulations. The FDA and certain foreign regulatory

authorities, such as the EMA, require preclinical studies to be conducted in accordance with applicable good laboratory practices and clinical trials to be conducted in accordance with applicable FDA regulations and applicable good clinical practices, including requirements for conducting, recording and reporting the results of preclinical studies and clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. Any such event could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

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

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

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

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

We expect to continue to rely on third-party manufacturers if we receive regulatory approval for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. If we are

unable to obtain or maintain third-party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third party's failure to execute on our manufacturing requirements could adversely affect our business in a number of ways, including:

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

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

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

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

The development and commercialization of drugs is highly competitive. We compete with a variety of multinational pharmaceutical companies and specialized biotechnology companies, as well as technology being

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

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

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

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

Our success largely depends on the continued service of key management and other specialized personnel, including: Douglas M. Fambrough, III, Ph.D., our chief executive officer; Bob D. Brown, Ph.D., our chief scientific officer; Ralf Rosskamp, M.D., our chief medical officer; John B. Green, our chief financial officer; and James B. Weissman, our chief business officer. The loss of one or more members of our management team or other key employees or advisors could delay our research and development programs and materially harm our business, financial condition, results of operations and prospects. The relationships that our key managers have cultivated within our industry make us particularly dependent upon their continued employment with us. We are dependent on the continued service of our technical personnel because of the highly complex nature of our product candidates and technologies and the specialized nature of the regulatory approval process. Because our management team and key employees are not obligated to provide us with continued service, they could terminate their employment with us at any time without penalty. We do not maintain key person life insurance

policies on any of our management team members or key employees. Our future success will depend in large part on our continued ability to attract and retain other highly qualified scientific, technical and management personnel, as well as personnel with expertise in clinical testing, manufacturing, governmental regulation and commercialization. We face competition for personnel from other companies, universities, public and private research institutions, government entities and other organizations.

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

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

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

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

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

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

Even if we receive marketing and commercialization approval of a product candidate, we and our third-party services providers will be subject to continuing regulatory requirements, including a broad array of regulations related to establishment registration and product listing, manufacturing processes, risk management measures, quality and pharmacovigilance systems, post-approval clinical studies, labeling, advertising and promotional activities, record keeping, distribution, adverse event reporting, import and export of pharmaceutical

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

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

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

In some countries, particularly member states of the EU, the pricing of prescription drugs may be subject to governmental control, at national as well as at regional levels. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a product. In addition, in the U.S. and elsewhere, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing and reimbursement negotiations, and pricing

negotiations may continue after coverage or reimbursement has been obtained. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we or our collaborators may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our RNAi therapeutic candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of any product candidate approved for marketing is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, financial condition, results of operations or prospects could be adversely affected.

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

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

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

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

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

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

If we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected.

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

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

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

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

Our current operations are located in our facilities situated in Cambridge. Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, power shortage, telecommunication failure or other natural or manmade accidents or incidents that prevent us from fully utilizing

the facilities, may have a material adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our product candidates or interruption of our business operations. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Any business interruption may have a material adverse effect on our business, financial position, results of operations and prospects.

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

We have incurred substantial losses during our history, do not expect to become profitable for the foreseeable future and may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. We may be unable to use these losses to offset income before such unused losses expire. Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50 percentage point change by value in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be further limited. We have not performed an analysis on whether we have experienced any ownership changes in the past. It is possible that we have experienced an ownership change, including pursuant to the initial public offering of our common stock, which closed on February 4, 2014, our follow-on offering of common stock in 2015, the 2017 Offering and the issuance of common stock in connection with the conversion of our Redeemable Convertible Preferred, and that our net operating losses are subject to such limitation. As of December 31, 2017, we had significant U.S. federal and Massachusetts net operating loss carryforwards. Any limit on these loss carryforwards if we have or do experience an ownership change could have an adverse effect on our business, financial position, results of operations and prospects.

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

As of December 31, 2017, we had $113.7 million in cash and cash equivalents and held-to-maturity investments. We historically have invested substantially all of our available cash and cash equivalents in corporate bonds, commercial paper, securities issued by the U.S. government, certificates of deposit and money market funds meeting the criteria of our investment policy, which is focused on the preservation of our capital. These investments are subject to general credit, liquidity, market and interest rate risks. For example, the impact of U.S. sub-prime mortgage defaults in recent years affected various sectors of the financial markets and caused credit and liquidity issues. We may realize losses in the fair value of these investments or a complete loss of these investments, which would have a negative effect on our consolidated financial statements.

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

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

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

Risks Related to Intellectual Property

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

Our success depends in part on our ability to obtain and maintain patents and other forms of intellectual property rights, including in-licenses of intellectual property rights of others, for our product candidates, methods used to manufacture our product candidates and methods for treating patients using our product candidates, as well as our ability to preserve our trade secrets, to prevent third parties from infringing upon our proprietary rights and to operate without infringing upon the proprietary rights of others. There can be no assurance that an issued patent will remain valid and enforceable in a court of law through the entire patent term. Should the validity of a patent be challenged, the legal process associated with defending the patent may be costly and time consuming. Issued patents can be subject to oppositions, interferences, post-grant proceedings, and other third-party challenges that can result in the revocation of the patent or limit patent claims such that patent coverage lacks sufficient breadth to protect subject matter that is commercially relevant. Competitors may be able to circumvent our patents. Development and commercialization of pharmaceutical products can be subject to substantial delays and it is possible that at the time of commercialization any patent covering the product will have expired or will be in force for only a short period of time thereafter.

As of March 7, 2018, our worldwide patent estate, not including the patents and patent applications that we have licensed from third parties, included over 35 issued patents or allowed patent applications and over 100 pending patent applications supporting commercial development of our RNAi molecules and delivery technologies. We may not be able to apply for patents on certain aspects of our product candidates or delivery technologies in a timely fashion or at all. Our existing issued and granted patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing products and technology. There is no guarantee that any of our pending patent applications will result in issued or granted patents, that any of our issued or granted patents will not later be found to be invalid or unenforceable or that any issued or granted patents will include claims that are sufficiently broad to cover our product candidates or delivery technologies or to provide meaningful protection from our competitors. Moreover, the patent position of biotechnology and pharmaceutical companies can be highly uncertain because it involves complex legal and factual questions. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our current and future proprietary technology and product candidates are covered by valid and enforceable patents or are effectively maintained as trade secrets. If third parties disclose or misappropriate our proprietary rights, it may materially and adversely impact our position in the market.

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

In addition, there are numerous recent changes to the patent laws and proposed changes to the rules of the USPTO which may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, the Leahy-Smith America Invents Act enacted in 2011 involves significant changes in patent legislation. The U.S. Supreme Court has ruled on several patent cases in recent years, some of which cases either narrow the scope of patent protection available in certain circumstances or weaken the rights of patent owners in certain situations. The 2013 decision by the U.S. Supreme Court in *Association for Molecular*

Pathology v. Myriad Genetics, Inc. precludes a claim to a nucleic acid having a stated nucleotide sequence which is identical to a sequence found in nature and unmodified. We currently are not aware of an immediate impact of this decision on our patents or patent applications because we are developing nucleic acid products that are not found in nature. However, this decision has yet to be clearly interpreted by courts and by the USPTO. We cannot assure you that the interpretations of this decision or subsequent rulings will not adversely impact our patents or patent applications. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing U.S. patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

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

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

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

Research and development of RNAi-based therapeutics and other oligonucleotide-based therapeutics has resulted in many patents and patent applications from organizations and individuals seeking to obtain patent protection in the field. Our efforts are based on RNAi technology that we have licensed and that we have developed internally and own or co-own. We have chosen this approach to increase our likelihood of technical success and our freedom to operate. We have obtained grants and issuances of RNAi-based patents and have licensed other patents from third parties on exclusive and non-exclusive bases. The issued patents and pending patent applications in the U.S. and in key markets around the world that we own, co-own or license claim many

different methods, compositions and processes relating to the discovery, development, manufacture and commercialization of RNAi therapeutics. Specifically, we own, co-own or have licensed a portfolio of patents, patent applications and other intellectual property covering: (1) certain aspects of the structure and uses of RNAi molecules, including their manufacture and use as therapeutics, and RNAi-related mechanisms, (2) chemical modifications to RNAi molecules that improve their properties and suitability for therapeutic uses, (3) RNAi molecules directed to specific gene sequences and drug targets as treatments for particular diseases and (4) delivery technologies, such as in the field of lipid nanoparticles and lipid nanoparticle formulation, and chemical modifications such as conjugation to targeting moieties.

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

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

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

events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

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

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

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

We do, and will continue to, rely on intellectual property rights licensed from third parties to protect our technology, including licenses that give us rights to third-party intellectual property that is necessary or useful for our business. 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 certain of our rights under our third-party licenses to BI and may sublicense such rights to current or future collaborators. Any impairment of these sublicensed rights could result in reduced revenue under our collaboration agreement with BI or result in termination of an agreement by one or more of our existing or any other future collaborators.

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

To the extent that we do not have exclusive rights in the patents covered by the license granted to us by COH, we cannot prevent third parties from developing DsiRNA based product candidates in competition with certain of our GalXC products. Prior to entering into the license with us, COH had entered into a non-exclusive

license with a third party with respect to such patent rights to manufacture, use, import, offer for sale and sell products covered by the licensed patent rights for the treatment or prevention of disease in humans (excluding viruses and delivery of products into the eye or ear). While we believe that such non-exclusive license has been terminated, COH has informed us that a sublicensee to that non-exclusive license was permitted to enter into an equivalent non-exclusive license which, to our knowledge, is subsisting with Arrowhead, as successor to the non-exclusive license holder. As successor to the non-exclusive license holder, we believe that Arrowhead has substantially similar access to the same patent rights related to technology granted to us under our license with COH. Arrowhead is developing RNA-based therapeutics for the treatment of diseases of the liver, which may directly compete with our product candidates. In addition, the U.S. government has certain rights to the inventions covered by the patent rights and COH, as an academic research and medical center, has the right to practice the licensed patent rights for educational, research and clinical uses. If Arrowhead or another party develops, manufactures, markets and sells any product covered by the same patent rights and technologies that compete with ours, it could significantly undercut the value of any of our product candidates, which would materially and adversely affect our revenue, financial condition and results of operations.

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

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

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

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

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

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

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

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

Our current licenses impose, and any future licenses we enter into are likely to impose, various development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement, and other obligations on us. If we breach any of these obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages and the licensor may have the right to terminate the license, which could result in us being unable to develop, manufacture and sell products that are covered by the licensed technology or enable a competitor to gain access to the licensed technology. Moreover, our licensors may own or control intellectual property that has not been

licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

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

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

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

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

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

Responding to these allegations can be costly and disruptive to our business, even when the allegations are without merit, and can be a distraction to management. On June 10, 2015, Alnylam filed a complaint against us in the Superior Court of Middlesex County, Massachusetts (the "Court"). The complaint alleges misappropriation of confidential, proprietary, and trade secret information, as well as other related claims, in connection with our hiring of a number of former employees of Merck and our discussions with Merck regarding the acquisition of its subsidiary, Sirna, which was subsequently acquired by Alnylam. Alnylam seeks, among other things, damages in excess of $100.0 million, attorneys' fees, and an order permanently enjoining the Company from disclosing or using any of Alnylam's confidential information or trade secrets. The Court has set a trial date of April 23, 2018.

This matter has caused us to incur significant legal fees and other costs to defend against this action and will continue to do so through the trial and potentially beyond. We believe, however, that Alnylam's allegations lack merit. In response to the complaint, we filed an answer denying all liability, and we will continue to vigorously defend all claims asserted. We expect that a finding of liability against us is not probable. Accordingly, we cannot reasonably estimate any range of potential future charges, and we have not recorded any accrual for a contingent liability associated with this legal proceeding. However, an unfavorable resolution could potentially have a material adverse effect on our business, financial condition, and results of operations or prospects, potentially delay or limit our ability to use some of our research and development programs, and potentially result in paying monetary damages. In addition, if an unfavorable resolution had a material adverse impact on our ability to meet our obligations under the BI Agreement, we could be required to repay to BI certain future milestone payments, excluding the upfront payment, R&D reimbursement and certain other payments paid or to be paid to us by BI. As we believe Alnylam's suit is without merit and intended only to cause competitive harm, we filed a countersuit in the case against Alnylam for damages, and on August 8, 2017, we filed a complaint in the Federal District court for the District of Massachusetts asserting a federal antitrust claim against Alnylam.

We may be subject to additional claims in the future that these or other employees of the Company have, or we have, inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending current or future claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, personnel, or the ability to use some of our research and development work. A loss of intellectual property, key research personnel, or their work product could hamper our ability to commercialize, or prevent us from commercializing, our product candidates, which could severely harm our business.

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

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

Risks Related to Government Regulation

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

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

We have very limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA as well as foreign regulatory authorities, such as the EMA. The time required to obtain FDA and foreign regulatory approvals is unpredictable but typically takes many years following the commencement of clinical trials, depending upon the type, complexity and novelty of the product candidate. The standards that the FDA and its foreign counterparts use when regulating us are not always applied predictably or uniformly and can change. Any analysis we perform of data from preclinical and clinical

activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also encounter unexpected delays or increased costs due to new government regulations, for example, from future legislation or administrative action, or from changes in the policy of the FDA or foreign regulatory authorities during the period of product development, clinical trials and regulatory review by the FDA or foreign regulatory authorities. It is impossible to predict whether legislative changes will be enacted, or whether FDA or foreign laws, regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be.

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

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

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

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

Although we do not currently have any products on the market, once we begin commercializing our therapeutic candidates, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal, state and foreign governments of the jurisdictions in which we conduct our business. Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any therapeutic candidates for which we obtain marketing approval. Our future arrangements with third party payors and customers may expose us to broadly applicable fraud and abuse, transparency, and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships

through which we market, sell and distribute our therapeutic candidates for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include, but are not limited to, the following:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons from soliciting, receiving, offering or providing remuneration, directly or indirectly, to induce either the referral of an individual for a healthcare item or service, or the purchasing or ordering of an item or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare or Medicaid;
- federal civil and criminal false claims laws and civil monetary penalty laws, such as the U.S. federal FCA, which imposes criminal and civil penalties, including through civil whistleblower or *qui tam* actions, against, individuals or entities for knowingly presenting or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA;
- HIPAA includes a fraud and abuse provision referred to as the HIPAA All-Payor Fraud Law, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by HITECH, and its implementing regulations, which impose obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding, 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;
- federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- the federal Physician Payment Sunshine Act and the implementing regulations, also referred to as "Open Payments," issued under the ACA, which require that manufacturers of pharmaceutical and biological drugs reimbursable under Medicare, Medicaid, and Children's Health Insurance Programs report to the Department of Health and Human Services all consulting fees, travel reimbursements, research grants, and other payments, transfers of value or gifts made to physicians and teaching hospitals with limited exceptions; and
- Analogous state laws and regulations, such as, state anti-kickback and false claims laws potentially applicable to sales or marketing arrangements and claims involving healthcare items or services reimbursed by nongovernmental third party payors, including private insurers; and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal

and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Responding to investigations can be time-and resource-consuming and can divert management's attention from the business. Any such investigation or settlement could increase our costs or otherwise have an adverse effect on our business.

Ensuring that our future business arrangements with third-parties comply with applicable healthcare laws and regulations could involve substantial costs. 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, 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.

If we or current or future 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;
- a corporate integrity agreement;
- 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 coverage and reimbursement practices or healthcare reform initiatives, thereby harming our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drugs vary widely from country to country. Some countries require approval of the sale price of a drug before it can be

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

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. However, there may be significant delays in obtaining coverage for newly-approved drugs. Moreover, eligibility for coverage does not necessarily signify that a drug will be reimbursed in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution costs. Also, interim payments for new drugs, if applicable, may be insufficient to cover our costs and may not be made permanent. Thus, even if we succeed in bringing one or more products to the market, these products may not be considered medically necessary or 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. In addition, obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our product on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize any product candidate that we successfully develop.

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 Medicare through Medicare Part B. Specifically, Medicare Part B coverage may be available for eligible beneficiaries when the following, among other requirements have been satisfied:

- the product is reasonable and necessary for the diagnosis or treatment of the illness or injury for which the product is administered according to accepted standards of medical practice;
- the product is typically furnished incident to a physician's services;
- the indication for which the product will be used is included or approved for inclusion in certain Medicare-designated pharmaceutical compendia (when used for an off-label use); and
- the product has been approved by the FDA.

Average prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S. Reimbursement rates under Medicare

Part B would depend in part on whether the newly approved product would be eligible for a unique billing code. Self-administered, outpatient drugs are typically reimbursed under Medicare Part D, and drugs that are administered in an inpatient hospital setting are typically reimbursed under Medicare Part A under a bundled payment. It is difficult for us to predict how Medicare coverage and reimbursement policies will be applied to our products in the future and coverage and reimbursement under different federal healthcare programs are not always consistent. Medicare reimbursement rates may also reflect budgetary constraints placed on the Medicare program.

Third party payors often rely upon Medicare coverage policies and payment limitations in setting their own reimbursement rates. These coverage policies and limitations may rely, in part, on compendia listings for approved therapeutics. Our inability to promptly obtain relevant compendia listings, coverage, and adequate reimbursement 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 expect that these and other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drugs, once marketing approval is obtained.

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., in 2010, the U.S. Congress passed the ACA, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of health spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional policy reforms.

Among the provisions of the ACA addressing coverage and reimbursement of pharmaceutical products, of importance to our potential therapeutic candidates are the following

- increases to pharmaceutical manufacturer rebate liability under the Medicaid Drug Rebate Program due to an increase in the minimum basic Medicaid rebate on most branded prescription drugs and the application of Medicaid rebate liability to drugs used in risk-based Medicaid managed care plans;
- the expansion of the 340B Drug Pricing Program 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;
- requirements imposed on 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”;
- requirements imposed on pharmaceutical companies 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 currently expect our branded pharmaceutical sales to constitute a small portion of the total federal healthcare program pharmaceutical market, we do not currently expect this annual assessment to have a material impact on our financial condition; and

- For products classified as biologics, 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, it may be possible for biosimilar manufacturers 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.

Separately, pursuant to the health reform legislation and related initiatives, the Centers for Medicare and Medicaid Services ("CMS") is working with various healthcare providers to develop, refine, and implement Accountable Care Organizations ("ACOs"), and other innovative models of care for Medicare and Medicaid beneficiaries, including the Bundled Payments for Care Improvement Initiative, the Comprehensive Primary Care Initiative, the Duals Demonstration, and other models. The continued development and expansion of ACOs and other innovative models of care will have an uncertain impact on any future reimbursement we may receive for approved therapeutics administered by such organizations

From time to time, legislation is drafted, introduced and passed in the U.S. Congress that could significantly change the statutory provisions governing coverage, reimbursement, and marketing of products regulated by CMS or other government agencies. In addition to new legislation, CMS coverage and reimbursement policies are often revised or interpreted in ways that may significantly affect our business and our products.

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

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

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Our practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor.

Additionally, the intent standard under the Anti-Kickback Statute was amended by the ACA, to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA codified case law that a claim including items or services resulting from a violation of the federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the federal FCA (discussed below).

The civil monetary penalties statute imposes penalties against any person or entity that, among other things, is determined to have presented or caused to be presented a claim to a federal healthcare program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

Federal false claims and false statement laws, including the federal FCA, prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment to, or approval by, the federal healthcare programs, including Medicare and Medicaid, or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. For instance, historically, pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, off-label, and thus generally non-reimbursable, uses.

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 we act as a business associate to a healthcare provider engaging in electronic transactions, we may also be subject to the privacy and security provisions of HIPAA, as amended by HITECH, which restricts the use and disclosure of patient-identifiable health information, mandates the adoption of standards relating to the privacy and security of patient-identifiable health information, and requires the reporting of certain security breaches to healthcare provider customers with respect to such information. Additionally, many states have enacted similar laws that may impose more stringent requirements on entities like ours. Failure to comply with applicable laws and regulations could result in substantial penalties and adversely affect our financial condition and results of operations.

Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Additionally, to the extent that our product is sold in a foreign country, we may be subject to similar foreign laws

Certain Dicerna products, one approved, may be eligible for coverage under Medicare and Medicaid, among other government healthcare programs. Accordingly, Dicerna may be subject to a number of obligations based on its participation in these programs, such as a requirement to calculate and report certain price reporting metrics to the government, such as average sales price and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. It is difficult to predict how Medicare coverage and reimbursement policies will be applied to Dicerna's 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.

In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of drug and biological products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no

place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical and biotechnology companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical and biotechnology companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including without limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private "qui tam" actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Our ability to obtain 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 (the "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, referred to as 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 2015 extended sequestration for Medicare through fiscal year 2027.

The U.S. federal budget remains in flux, which could, among other things, cut Medicare payments to providers. The Medicare program is frequently mentioned as a target for spending cuts. The full impact on our business of any future cuts in Medicare or other programs is uncertain. In addition, we cannot predict any impact President Trump's administration and the U.S. Congress may have on the federal budget. If federal spending is reduced, anticipated budgetary shortfalls may also impact the ability of relevant agencies, such as the FDA or the 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 receive marketing approval and we or others later identify undesirable side effects caused by the product candidate, our ability to market and derive revenue from the product candidates could be compromised.

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

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

Risks Related to Our Common Stock

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

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

in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our share price may be more volatile.

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

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

Our stock price is volatile. From January 30, 2014, the first day of trading of our common stock, through March 7, 2018, the closing sale price of our common stock has ranged between a high of $46.00 per share and a low of $2.45 per share. The market price for our common stock may be influenced by many factors, including the other risks described in this "Risk Factors" section and the following:

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

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

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

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

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

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

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

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

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

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

As of December 31, 2017, our executive officers and directors, together with holders of five percent or more of our outstanding common stock and their respective affiliates, beneficially owned, in the aggregate, approximately 69% of our outstanding common stock, including common shares resulting from the conversion of the Redeemable Convertible Preferred, and subject to outstanding options and warrants that are exercisable within 60 days after such date, based on the Forms 3 and 4 and Schedules 13D and 13G filed by them with the SEC. As a result, these stockholders, if acting together, will continue to have significant influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets and any other significant corporate transaction. The interests of these stockholders may not be the same as, or may even conflict with the interests of our other stockholders. For example, these stockholders could delay or prevent a change of control of our Company, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our Company or our assets and might affect the prevailing market price of our common stock. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

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

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

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

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

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

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

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

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

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

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

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

Our stock price has fluctuated and may fluctuate for many reasons, including as a result of public announcements regarding the progress of our development efforts or the development efforts of our collaborators or competitors, the addition or departure of our key personnel, variations in our quarterly operating results and changes in market valuations of pharmaceutical and biotechnology companies. This risk is especially relevant to us because pharmaceutical and biotechnology companies have experienced significant stock price volatility in recent years. When the market price of a stock has been volatile as our stock price has been and may be, holders

of that stock have occasionally brought securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit of this type against us, even if the lawsuit is without merit, we could incur substantial costs defending the lawsuit. The lawsuit could also divert the time and attention of our management.

Our amended and restated bylaws designate 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, as we did with the Redeemable Convertible Preferred, which was converted into common stock in December 2017. 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 allowing the purchase of our common stock. As of March 7, 2018, we also had 1,879,470 shares of common stock reserved for future issuance under our stock incentive plans. As of that date, there were also stock options and awards to purchase 7,216,127 shares of our common stock outstanding and warrants to purchase 87,901 shares of our common stock outstanding. The exercise of outstanding options and 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 March 7, 2018, we had 51,766,999 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.

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

In connection with the Private Placement, we issued 700,000 shares of the Redeemable Convertible Preferred, which were convertible into shares of our common stock at an agreed conversion rate. In December 2017, all shares of Redeemable Convertible Preferred were converted into 24,206,663 shares of our common stock. We have agreed to grant the holders of Redeemable Convertible Preferred certain demand, shelf and "piggyback" registration rights with respect to the shares of common stock issued upon conversion of the Redeemable Convertible Preferred. Such registration rights continue subsequent to the conversion and repurchase of the Redeemable Convertible Preferred with respect to the shares of common stock issued in such conversion. Upon the effectiveness of such registration statements, all shares of common stock issued upon conversion of the Redeemable Convertible Preferred may be freely sold in the open market. The sale of a significant amount of these shares in the open market or the perception that these sales may occur could cause the market price of our common stock to decline or become highly volatile.

Item 1B. *Unresolved Staff Comments*

None.

Item 2. *Properties*

Our corporate headquarters are located in Cambridge, Massachusetts, where we lease 37,084 square feet of office and laboratory space. The lease term for our office and laboratory space in Cambridge, Massachusetts, commenced in December 2014 for a lease term of six years.

We believe that suitable additional or alternative space will be available as needed on commercially reasonable terms.

Item 3. *Legal Proceedings*

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

On June 10, 2015, Alnylam filed a complaint against the Company in the Superior Court of Middlesex Country, Massachusetts (the "Court"). The complaint alleges misappropriation of confidential, proprietary, and trade secret information, as well as other related claims, in connection with the Company's hiring of a number of former employees of Merck and its discussions with Merck regarding the acquisition of its subsidiary, Sirna, which was subsequently acquired by Alnylam. Alnylam seeks, among other things, damages in excess of $100.0 million, attorneys' fees, and an order permanently enjoining the Company from disclosing or using any of Alnylam's confidential information or trade secrets. The Court has set a trial date of April 23, 2018. This matter has caused us to incur significant legal fees and other costs to defend against this action and will continue to do

so through the trial and potentially beyond. We believe, however, that Alnylam's allegations lack merit. In response to the complaint, we filed an answer denying all liability, and we will continue to vigorously defend all claims asserted. We expect that a finding of liability against us is not probable. Accordingly, we cannot reasonably estimate any range of potential future charges, and we have not recorded any accrual for a contingent liability associated with this legal proceeding. However, an unfavorable resolution could potentially have a material adverse effect on our business, financial condition, and results of operations or prospects, potentially delay or limit our ability to use some of our research and development programs, and potentially result in paying monetary damages. Additionally, as we believe Alnylam's suit is without merit and intended only to cause competitive harm, we filed a countersuit in the case against Alnylam for damages, and on August 8, 2017, we filed a complaint in the Federal District Court for the District of Massachusetts asserting a federal antitrust claim against Alnylam.

Item 4. ***Mine Safety Disclosures***

Not applicable.

PART II

Item 5. ***Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities***

Market Information for Common Stock

Our common stock trades on The NASDAQ Global Select Market under the symbol "DRNA." The following table sets forth the high and low sale prices per share for our common stock on The NASDAQ Global Select Market for the periods indicated:

Year Ended December 31, 2017	High	Low
First Quarter	$ 3.40	$2.42
Second Quarter	$ 3.85	$2.87
Third Quarter	$ 5.82	$2.69
Fourth Quarter	$10.24	$4.91

Year Ended December 31, 2016	High	Low
First Quarter	$12.05	$4.30
Second Quarter	$ 5.85	$2.69
Third Quarter	$ 6.10	$3.00
Fourth Quarter	$ 5.98	$2.74

Holders of Record

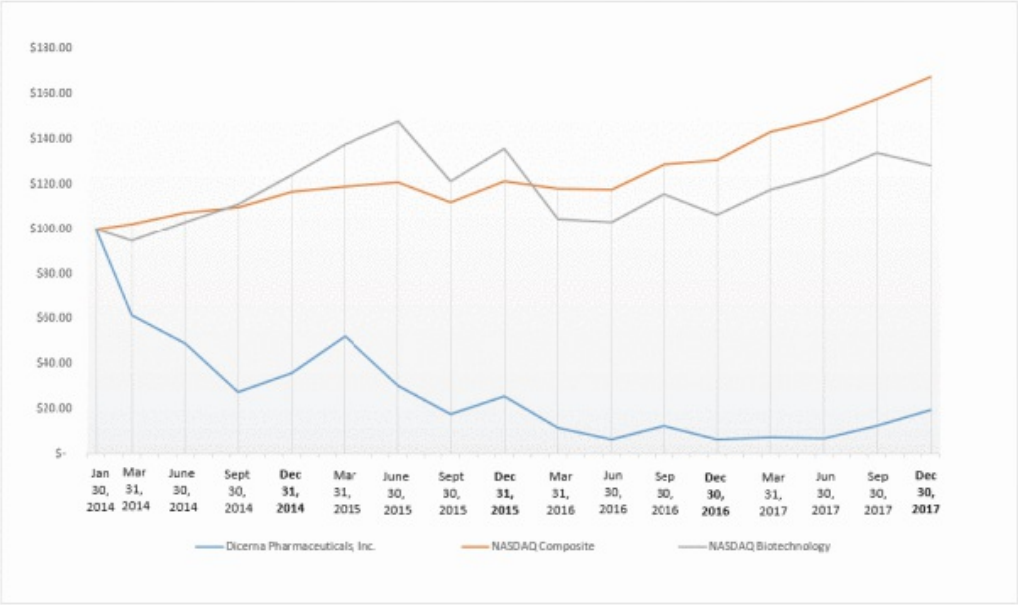
As of March 7, 2018, there were approximately 27 holders of record of our common stock. Because many of our shares of common stock are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of beneficial stockholders represented by these record holders.

Dividend Policy

We currently intend to retain future earnings, if any, for use in the operation of our business and to fund future growth. We have never declared or paid cash dividends on our common stock and we do not intend to pay any cash dividends on our common stock for the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors in light of conditions then existing, including factors such as our results of operations, financial condition and requirements, business conditions and covenants under any applicable contractual arrangements.

Performance Graph

The following graph illustrates a comparison of the total cumulative stockholder return on our common stock since January 30, 2014 (the date our stock became publicly traded on The NASDAQ Global Select Market) to the NASDAQ composite and NASDAQ biotechnology indices. The graph assumes an initial investment of $100 on January 30, 2014. The stock price performance on the following graph is not necessarily indicative of future stock price performance. This performance graph shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or incorporated by reference into any of our filings under the Securities Act or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.



Recent Sales of Unregistered Securities

On April 11, 2017, we issued and sold 700,000 shares of our newly designated Redeemable Convertible Preferred to the Preferred Holders at a purchase price of $100.00 per share, for total gross proceeds of $70.0 million. On December 18, 2017, all shares of Redeemable Convertible Preferred, including the value of cumulative dividends thereon, were converted into an aggregate of 24,206,663 shares of our common stock. The sale and issuance of shares of common stock upon exercise and conversion of the Redeemable Convertible Preferred were offered and sold by us pursuant to an exemption from the registration requirements of the Securities Act provided by Section 4(a)(2) thereunder. Each Preferred Holder represented that it was an "accredited investor" as defined in Regulation D promulgated under the Securities Act, that such securities were being acquired for its own account for investment and not with a view toward distribution in a manner which would violate the Securities Act and that they could bear the economic risks of the investment. Appropriate legends were affixed to the instruments representing the securities issued in such transaction. See "Item 1—Business, Corporate Developments" for a more detailed discussion of the issuance and conversion of the Redeemable Convertible Preferred.

Use of Proceeds from Initial Public Offering of Common Stock

Not applicable.

Purchases of Equity Securities by the Issuer and Affiliated Parties

None.

Item 6. ***Selected Financial Data***

DICERNA PHARMACEUTICALS, INC. AND SUBSIDIARIES
SELECTED FINANCIAL DATA
(In thousands, except for share and per share data)

	YEARS ENDED DECEMBER 31,				
	2017	**2016**	**2015**	**2014**	**2013**
Results of operations data					
Revenue from collaborative arrangement	$ 1,182	$ —	$ —	$ —	$ —
Grant revenue	1,095	295	184	—	—
Total revenue	2,277	295	184	—	—
Operating expenses:					
Research and development	36,983	41,694	43,971	29,453	11,558
General and administrative	25,881	18,349	19,240	15,648	5,820
Total operating expenses	62,864	60,043	63,211	45,101	17,378
Loss from operations	(60,587)	(59,748)	(63,027)	(45,101)	(17,378)
Other income (expense):					
Preferred stock warrant remeasurement	—	—	—	(2,559)	126
Loss on extinguishment of debt	—	—	—	(143)	(318)
Interest income	539	235	188	63	4
Interest expense	—	—	—	(199)	(952)
Total other income (expense)	539	235	188	(2,838)	(1,140)
Net loss	(60,048)	(59,513)	(62,839)	(47,939)	(18,518)
Dividends on redeemable convertible preferred stock	(10,111)	—	—	(204)	(2,388)
Deemed dividend related to beneficial conversion feature of redeemable convertible preferred stock	(6,144)	—	—	—	—
Deemed dividend on conversion of redeemable convertible preferred stock	(3,837)	—	—	—	—
Net loss attributable to common stockholders	$ (80,140)	$ (59,513)	$ (62,839)	$ (48,143)	$(20,906)
Net loss per share attributable to common stockholders—basic and diluted	$ (3.66)	$ (2.87)	$ (3.09)	$ (3.00)	$(709.57)
Weighted average common shares outstanding—basic and diluted	21,917,415	20,719,761	20,320,628	16,070,054	29,463
Financial condition data					
Cash and cash equivalents	$ 68,789	$ 20,865	$ 56,058	$ 26,067	$ 46,595
Held-to-maturity investments	$ 44,889	$ 25,009	$ 38,551	$ 72,556	$ —
Total assets	$ 120,884	$ 51,252	$ 100,023	$ 103,605	$ 49,794
Long-term debt—net of current portion	$ —	$ —	$ —	$ —	$ 260
Total stockholders' equity (deficit)	$ 101,238	$ 41,208	$ 91,022	$ 98,340	$(68,919)

The preceding selected consolidated financial data have been derived from our audited consolidated financial statements. Our audited consolidated financial statements as of December 31, 2017 and 2016 and for the fiscal years ended December 31, 2017, 2016 and 2015 are included elsewhere in this Annual Report on Form 10-K. The information set forth above should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations," included in Item 7 of this Annual Report on Form 10-K, and with our consolidated financial statements and notes thereto, included in Item 8 of this Annual Report on Form 10-K. The information set forth above is not necessarily indicative of our future results of operations or financial condition.

Item 7. ***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 I, Item 1A—"Risk Factors."

Overview

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

All of our GalXC drug discovery and development efforts are based on the therapeutic modality of RNAi, a highly potent and specific mechanism for silencing the activity of a targeted gene. In this naturally occurring biological process, double-stranded RNA molecules induce the enzymatic destruction of the messenger ribonucleic acid ("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. Our GalXC RNAi platform utilizes a particular structure of double-stranded RNA molecules configured for subcutaneous delivery to the liver. Due to the enzymatic nature of RNAi, a single GalXC molecule incorporated into the RNAi machinery can destroy hundreds or thousands of mRNAs from the targeted gene.

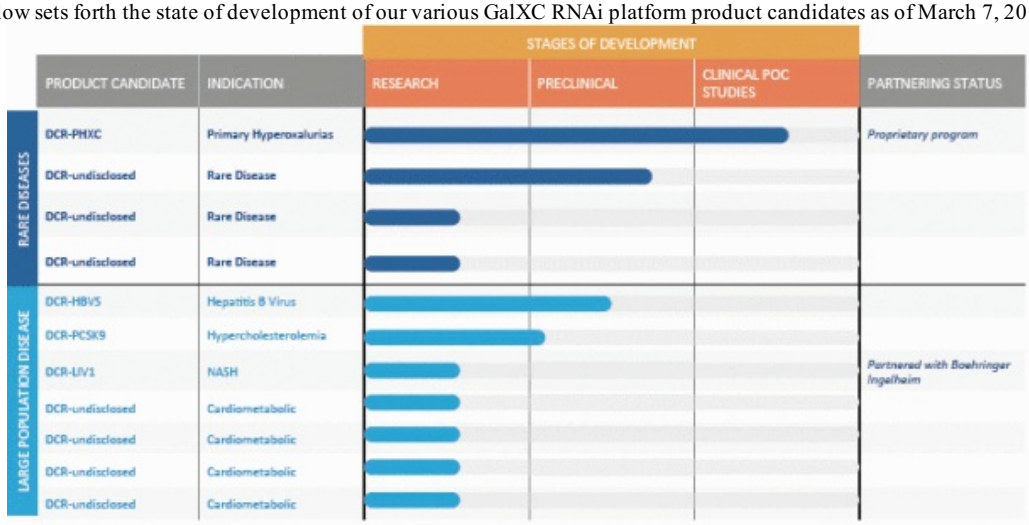
The GalXC RNAi platform supports Dicerna's long-term strategy to retain, subject to the evaluation of potential licensing opportunities as they may arise, a full or substantial ownership stake and to invest internally in diseases with focused patient populations, such as certain rare diseases. We see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

Development Programs

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

GalXC product candidate, DCR-PHXC, with the Medicines and Healthcare products Regulatory Agency ("MHRA") in the United Kingdom ("UK"), and in December 2017, we dosed the first human in the Phase 1 DCR-PHXC clinical trial. We expect to file additional CTAs and/or INDs for our programs in 2018 and 2019.

The table below sets forth the state of development of our various GalXC RNAi platform product candidates as of March 7, 2018.



Our current GalXC RNAi platform development programs are as follows:

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

  On October 16, 2017, we announced that we had submitted a CTA for DCR-PHXC to the MHRA in the UK. On December 7, 2017, we announced that we dosed the first human in a Phase 1 trial of DCR-PHXC. The Phase 1 trial for DCR-PHXC, called PHYOX, is a single ascending-dose study of DCR-PHXC in normal healthy volunteers ("NHV") and patients with PH. The study is divided into two groups: Group A is a placebo-controlled, single-blind, single center Phase 1 study, enrolling up to 25 NHVs; Group B is an open-label, multi-center study enrolling up to 16 patients with PH types 1 ("PH1") and 2 ("PH2"). The primary objective of the study is to evaluate the safety and tolerability of single doses of DCR-PHXC in both groups. Secondary objectives are to characterize the pharmacokinetics of single doses of DCR-PHXC in NHVs and patients with PH, and to evaluate the pharmacodynamic effects of single doses of DCR-PHXC on biochemical markers including, but not limited to, changes in urine oxalate concentrations. Patients with PH will be dosed after safety has been established at the same dose level in normal healthy volunteers. We plan to dose the first patient in Group B in the second quarter of 2018 and expect to have clinical proof-of-concept ("POC") data in the second half of 2018. We have submitted CTAs in Germany, France and the Netherlands. Additionally, we expect to initiate a multi-dose Phase 2/3 study in the first quarter of 2019, pending positive POC data and regulatory approvals.

  On July 15, 2017, in a series of presentations at the 12th International Workshop on Primary Hyperoxaluria for Professionals, Patients and Families in Tenerife, Spain ("12th International Workshop"), we presented new preclinical data suggesting the potential utility of DCR-PHXC for

treating all forms of PH. In particular, we presented research from animal models demonstrating how DCR-PHXC inhibits the lactate dehydrogenase A ("LDHA") gene, which we have identified as potentially being an optimal therapeutic target in patients with PH. LDHA inhibition was shown in animal models to reduce oxalate to normal or near-normal levels in PH types 1, 2 and ethylene glycol-induced hyperoxaluria (a model for idiopathic PH).

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

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

- **An undisclosed rare disease involving the liver.** We are developing a GalXC-based therapeutic, targeting a liver-expressed gene involved in a serious rare disease. For competitive reasons, we have not yet publicly disclosed the target gene or disease. We have selected this target gene and disease based on criteria that include having a strong therapeutic hypothesis, a readily-identifiable patient population, the availability of a potentially predictive biomarker, high unmet medical need, favorable competitive positioning and what we believe is a rapid projected path to approval. The disease is a genetic disorder, where mutations in the disease gene lead to the production of an abnormal protein. The protein causes progressive liver damage and fibrosis, in some cases leading to cirrhosis and liver failure, and we believe that silencing of the disease gene will prevent production of the abnormal protein and thereby slow or stop progression of the liver fibrosis. Greater than 100,000 people in the United States ("U.S.") are believed to be homozygous (i.e. having identical pairs of genes for any given pair of hereditary characteristics) for the mutation that causes the liver disease, and at least 20% of those people, and potentially a significantly higher fraction, are believed to have liver-associated disease as a consequence. We plan to seek a risk-sharing collaborator for this program before we file an IND and/or CTA, which we expect to be prepared to file in the second quarter of 2018.
- **Chronic Hepatitis B Virus infection.** We have declared a GalXC RNAi platform-based product candidate for the treatment of HBV, DCR-HBVS, and are conducting formal non-clinical development studies. We expect to file an IND and/or a CTA during the fourth quarter of 2018. Current therapies for HBV rarely lead to a long-term immunological cure as measured by the clearance of HBV surface antigen ("HBsAg") and sustained HBV deoxyribonucleic acid ("DNA") suppression in patient plasma or blood. We expect to file an IND and/or a CTA during the fourth quarter of 2018. DCR-HBVS targets HBV messenger RNA, and leads to greater than 99% reduction in circulated HBsAg in mouse models of HBV infection. Based on these preclinical studies, and only if we receive appropriate regulatory approval to begin human clinical trials, we hope to determine the potential of DCR-HBVS to reduce HBsAg and HBV DNA levels in the blood of HBV patients in a commercially attractive subcutaneous dosing paradigm.
- **Hypercholesterolemia (PCSK9 targeted therapy).** We are using our GalXC RNAi platform to develop a therapeutic that targets the PCSK9 gene for the treatment of hypercholesterolemia. The Company has selected a provisional clinical candidate for the program, but is continuing to explore

ways to further optimize the program. PCSK9 is a validated target for hypercholesterolemia, and there are U.S. Food and Drug Administration ("FDA")-approved therapies targeting PCSK9 that are based on monoclonal antibody technology. Based on preclinical studies, we believe that our GalXC RNAi platform has the potential to produce a PCSK9-targeted therapy with attractive commercial properties, such as small subcutaneous injection volumes and less frequent dosing.

- **Additional pipeline programs.** We have developed a robust portfolio of additional targets and diseases that we plan to pursue either on our own or in collaboration with partners. We have applied our GalXC technology to multiple gene targets across our disease focus areas of rare diseases, chronic liver diseases and cardiovascular diseases. Pursuant to our strategy, we are seeking collaborations with larger pharmaceutical companies to advance our programs in the areas of chronic liver diseases and cardiovascular diseases. Both these disease areas represent large and diverse patient populations, requiring complex clinical development and commercialization paths that we believe can be more effectively pursued in collaboration with larger pharmaceutical companies. For our additional rare diseases, we are continuing to assess their potential for clinical success and market opportunity while optimizing our GalXC molecules. For our additional pipeline programs (including PCSK9), we may utilize more advanced versions of our GalXC technology, that further improve pharmaceutical properties of the GalXC molecules, including enhancing the duration of action and potency. We have further optimized our GalXC technology platform, enabling the development of next generation GalXC molecules. Improvements to our GalXC compound include modification of the tetraloop end of the molecule, which can be applied to any target gene and program, resulting in a substantially longer duration of action in animal models across multiple targets. Modification of the tetraloop only impacts the passenger strand and does not impact the guide strand. These modifications are unique to our GalXC molecules and, we believe, provide a competitive advantage for the Company.

In addition to the GalXC development programs outlined above, on October 27, 2017, we entered into a collaborative research and license agreement with Boehringer Ingelheim International GmbH, a wholly owned subsidiary of C.H. Boehringer Sohn AG & Co. KG ("BI") (the "BI Agreement"), pursuant to which the Company and BI jointly research and develop product candidates for the treatment of chronic liver diseases, with an initial focus on nonalcoholic steatohepatitis ("NASH") using our GalXC platform. NASH is caused by the buildup of fat in the liver, potentially leading to liver fibrosis and cirrhosis. NASH has an especially high prevalence among obese and diabetic patients and is an area of high unmet medical need. The BI Agreement is for the development of product candidates against one target gene with an option for BI to add the development of product candidates that target a second gene. We are working exclusively with BI to develop the product candidates against the undisclosed target gene. We are responsible for the discovery and initial profiling of the product candidates, including primary pre-clinical studies, synthesis, and delivery. BI is responsible for evaluating and selecting the product candidates for further development. If BI selects one or more product candidates, it will be responsible for further pre-clinical development, clinical development, manufacturing and commercialization of those products. Also pursuant to the BI Agreement, we granted BI a worldwide license in connection with the research and development of the product candidates and will transfer to BI intellectual property rights of the product candidates selected by BI for clinical development and commercialization. We also may provide assistance to BI in order to help BI further develop selected product candidates. Pursuant to the BI Agreement, BI agreed to pay us a non-refundable upfront payment of $10.0 million for the first target. During the term of the research program, BI will reimburse us the cost of materials and third-party expenses that have been included in the preclinical studies up to an agreed-upon limit. We are eligible to receive up to $191.0 million in potential development and commercial milestones related to the initial target. We are also eligible to receive royalty payments on potential global net sales, subject to certain adjustments, tiered from high single digits up to low double-digits. BI's option to add a second target would provide for an option fee payment and success-based development and commercialization milestones and royalty payments to us.

We are party to a collaboration for our early generation of non-GalXC Dicer Substrate 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 has provided us with notice of termination related to the non-KRAS program.

We also have developed a wholly owned clinical candidate, DCR-BCAT, targeting the ß-catenin oncogene. DCR-BCAT is based on an extended version of our earlier generation non-GalXC Dicer Substrate RNAi technology and is delivered by our lipid nanoparticle 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.

Corporate Developments

Underwritten public offering

On December 18, 2017, we completed an underwritten follow-on public offering of 5,714,286 shares of common stock (the "2017 Offering"). In connection with the 2017 Offering, we entered into an underwriting agreement (the "Underwriting Agreement") with Stifel, Nicolaus & Company, Incorporated and Evercore Group LLC as representatives of the underwriters listed in the Underwriting Agreement (collectively, the "Underwriters"), pursuant to which we granted to the Underwriters a 30-day option to purchase up to an additional 857,143 shares of the Company's common stock (the "Overallotment"). We completed the sale of 6,571,428 shares, including the exercise of the Overallotment, to the Underwriters on December 18, 2017, and that sale resulted in the receipt by the Company of aggregate gross proceeds of $46.0 million, less Underwriter commissions and additional offering expenses totaling approximately $3.2 million.

Redeemable Convertible Preferred Stock

Dicerna no longer has any outstanding shares of redeemable convertible preferred stock. On April 11, 2017, pursuant to an agreement with seven institutional investors (the "Preferred Holders"), led by funds advised by Bain Capital Life Sciences L.P. ("Lead Investor"), we issued and sold 700,000 shares of our newly designated redeemable convertible preferred stock (the "Redeemable Convertible Preferred") to the Preferred Holders in a private placement for aggregate gross proceeds of $70.0 million, less issuance costs of approximately $0.8 million (the "Private Placement"). In addition to the Lead Investor, other participants in the Private Placement included affiliates of Cormorant Asset Management, LLC, Domain Associates, LLC ("Domain Associates"), EcoR1 Capital, LLC, RA Capital Management, LLC ("RA Capital") and Skyline Management LLC ("Skyline Ventures"), among others. Domain Associates, RA Capital and Skyline Ventures are entities that are affiliated or were formerly affiliated with certain members of our board of directors.

On March 28, 2017, we increased the size of our board of directors from eight to nine directors and approved the appointment of Adam M. Koppel, M.D., Ph.D., a managing director of the Lead Investor, as a director of the Company, effective as of the closing of the Private Placement on April 11, 2017. Dr. Koppel was reelected to the Company's board of directors by shareholder vote in June 2017.

Each holder of Redeemable Convertible Preferred had been entitled to receive cumulative dividends on the Accrued Value, as defined below, of each share of Redeemable Convertible Preferred at an initial rate of 12% per annum, compounded quarterly and subject to two rate reductions, of 4% each in connection with the occurrence of certain agreed-upon milestone events. Entering into the BI Agreement constituted a milestone event for purposes of applying the first of two allowable rate reductions to dividends payable on the Redeemable Convertible Preferred. As such, the dividend rate on the Redeemable Convertible Preferred was reduced from 12% to 8%, effective on October 27, 2017. Dividends on the Redeemable Convertible Preferred accrued on the Accrued Value of each share of Redeemable Convertible Preferred until the conversion thereof, which occurred on December 18, 2017, as discussed below. "Accrued Value" meant, with respect to each share of Redeemable Convertible Preferred, the sum of (i) $100.00 plus (ii) on each quarterly dividend date, an additional amount equal to the dollar value of any dividends on a share of Redeemable Convertible Preferred which had accrued on any dividend payment date and had not previously been added to such Accrued Value.

On December 13, 2017, in connection with the 2017 Offering, we entered into a letter agreement (the "Letter Agreement") with the Preferred Holders. Pursuant to the Letter Agreement, the Preferred Holders agreed, subject to the completion of the offering, to optionally convert all of their shares of Redeemable Convertible Preferred into common stock. The Letter Agreement also provided for the Preferred Holders to waive and amend certain provisions in an amended and restated registration rights agreement by and among the Company and the Preferred Holders party thereto (the "Registration Rights Agreement"). In consideration for the Preferred Holders' agreeing to the optional conversion of the Redeemable Convertible Preferred and to a waiver under and certain amendments to the Registration Rights Agreement, we issued to the Preferred Holders shares of the Company's common stock. Under the Letter Agreement, the number of shares allocable to each Preferred Holder was calculated based on the number of shares of common stock into which the additional dividend accruals on the Redeemable Convertible Preferred that such Preferred Holders would have been entitled to receive up to and including March 31, 2018 would have been convertible, calculated immediately prior to the effectiveness of the conversion (the "Additional Investor Shares"). The formula for the Additional Investor Shares assumes (1) a conversion price of $3.19 per share of common stock; (2) application of a dividend rate of 12% per annum from April 11, 2017 to October 27, 2017 and (3) application of a dividend rate of 8% per annum commencing from October 28, 2017 through March 31, 2018. March 31, 2018 is approximately the date at which the Company expected to be able to force conversion of the Redeemable Convertible Preferred into shares of common stock, pursuant to the terms of the SPA. In addition to an increase in net loss per share attributable to common shareholders as a result of the recording of deemed and actual dividends, the ultimate impact of the April transaction on the Company's consolidated balance sheet and capital structure, excluding the impact of share issuance costs, was the receipt of $70 million of gross cash proceeds and the issuance of 24,206,663 common shares, or $2.89 per share. This compares to a closing per share price of the Company's common stock of $2.68 on March 28, 2017, the date of signing of the SPA.

On December 18, 2017, we completed the conversion of the Redeemable Convertible Preferred and issued an aggregate of 24,206,663 shares of our common stock, after which no shares of Redeemable Convertible Preferred remained outstanding. On December 29, 2017, we filed with the Secretary of State of the State of Delaware a Certificate of Elimination of the Redeemable Convertible Preferred, which eliminates from our Certificate of Incorporation all matters set forth in the Certificate of Designation of Redeemable Convertible Preferred Stock previously filed with the Secretary of State of the State of Delaware, which established and designated the Redeemable Convertible Preferred Stock and the rights, powers, preferences, privileges and limitations thereof.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the U.S. The preparation of our consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the revenue and expenses incurred during the reported periods. On an ongoing basis, we evaluate our estimates and judgments, including those related to revenue recognition, accrued expenses and, for 2017 only, in relation to the accounting for the Redeemable Convertible Preferred, including cumulative dividends thereon. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in the notes to our consolidated financial statements appearing in this Annual Report on Form 10-K, we believe that the following critical accounting policies are most important to understanding and evaluating our reported financial results.

Revenue recognition

We generate revenue from research collaboration and license agreements with third parties which contain multiple deliverables. The deliverables in the agreements include (a) the use of our technology and (b) research and development of product candidates. Such agreements may provide for consideration to the Company in the form of up-front payments, research and development services, option payments, milestone payments and royalties.

We recognize revenue for each unit of accounting when all of the following criteria have been met: (1) pervasive evidence of an arrangement exists; (2) delivery has occurred or services have been rendered and risk of loss has passed; (3) the seller's price to the buyer is fixed or determinable; and (4) collectibility is reasonably assured.

For multiple-element arrangements, we identify the deliverables included in the arrangement and determine whether the individual deliverables represent separate units of accounting or whether the deliverables must be accounted for as a combined unit of accounting. This evaluation involves subjective determinations and requires management to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting if the delivered item has value to the customer on a standalone basis and, if the arrangement includes a general right of return relative to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in our control. In assessing whether an item has standalone value, we consider factors such as the research, development, manufacturing and commercialization capabilities of the collaborator and the availability of the relevant expertise in the marketplace. In addition, we consider whether the collaborator can use a deliverable for its intended purpose without the receipt of the remaining deliverables, whether the value of the deliverable is dependent on the undelivered item and whether there are other vendors that could provide the undelivered items.

We consider whether options included in a collaborative arrangement are substantive. Options are considered substantive if, at the inception of the arrangement, we are at risk as to whether the collaborator will choose to exercise the option. Factors that we consider in evaluating whether an option is substantive include whether the optional elements are essential to the functionality of other programs nominated, whether economic factors compel the collaborator to purchase the optional elements, the cost to exercise the option, the overall objective of the arrangement and, the benefit the collaborator might obtain from the arrangement without exercising the option.

We recognize arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria are satisfied for that particular unit of accounting. In the event that a deliverable does not represent a separate unit of accounting, we recognize revenue from the combined unit of accounting over our contractual or estimated performance period for the undelivered elements, which is typically the term of our research and development obligations. If there is no discernible pattern of performance or if objectively measurable performance measures do not exist, we recognize revenue under the arrangement on a straight-line basis over the period we are expected to complete our performance obligations. Conversely, if the pattern of performance in which the service is provided to the customer can be determined and objectively measurable performance measures exist, then we recognize revenue under the arrangement using the proportional performance method. Revenue recognized is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the straight-line method or proportional performance method, as applicable, as of each consolidated balance sheet date.

When an option is considered substantive and there is no significant incremental discount, the option is not considered a deliverable in the arrangement and no consideration is allocated to it. Conversely, when an option is not considered substantive or it is considered substantive but is priced at an incremental discount, the option is analyzed to determine if it should be combined with other deliverables in the arrangement. Options that are

substantive and priced at a significant and incremental discount are further assessed to determine whether a portion of the upfront payment should be allocated to the option and other deliverables in the arrangement.

At the inception of an arrangement that includes milestone payments, we evaluate whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment as to whether: (1) the consideration is commensurate with either our performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from its performance to achieve the milestone; (2) the consideration relates solely to past performance; and (3) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. In making this assessment, management evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the particular milestone and the level of effort and investment required to achieve the milestone. There is considerable judgment involved in determining whether a milestone satisfies all of the criteria that define the milestone as substantive. Revenue from substantive milestones is recognized only upon successful achievement of the related milestone. Where milestones are not substantive, milestone payments are accounted for in the same manner as royalties, with revenue recognized upon achievement of the milestone, assuming all other revenue recognition criteria are met.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current portion of deferred revenue in our consolidated balance sheet. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

Non-refundable up-front license fees under the agreement are initially recorded as deferred revenue upon receipt and are recognized as revenue over our performance period as defined in the related agreement. Royalty payments are recognized as revenue based on contract terms and reported sales of licensed products, when reported sales are reliably measurable and collectibility is reasonably assured.

Research and development service revenue is recognized over the research term as the research and development services are provided. The cost of such services is reflected in research and development expenses in the period in which the expenses are incurred.

Grant revenue is recognized in the period during which the related grant research and activities are incurred and when there is reasonable assurance that (a) we will comply with any conditions attached to the grant and (b) the grant funding will be received. Costs associated with grants are included in research and development expenses in our consolidated statement of operations.

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 agreements with KHK and BI and from government grants. We have not generated any commercial product revenue, nor do we expect to generate any product revenue for the foreseeable future.

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 BI 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, to the extent achieved, 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, BI 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 and adversely affected.

Collaboration agreements

On October 27, 2017, we entered into the BI Agreement, as discussed above, pursuant to which, we were entitled to receive non-refundable upfront payment of $10.0 million, less a refundable withholding tax in Germany of $1.6 million. BI paid us $8.4 million during the fourth quarter of 2017. The non-refundable upfront payment was subject to a German withholding tax, which was withheld by BI and remitted to the German tax authority in accordance with local tax law. We expect to receive the remaining $1.6 million during the first half of 2018. During the year ended December 31, 2017, we recognized $1.2 million in revenue associated with the BI Agreement, including reimbursable third-party research expenses that are billable to BI.

The deliverables at the effective date of the BI Agreement include delivery of intellectual property, conducting agreed-upon research program services and providing BI the exclusive option right to reserve additional targets. The Company concluded the performance of additional research for any additional target, if the underlying target option is exercised by BI, is not a deliverable of the agreement at inception because it is a substantive option and is not priced at a significant and incremental discount. Milestone payments that are contingent upon our performance under the BI Agreement include developmental milestones totaling $39.0 million. We view these milestones as substantive and have excluded the amounts from allocable consideration at the outset of the arrangement. All potential commercial milestones, totaling $155.0 million, will be accounted for in the same manner as royalties and recorded as revenue upon achievement of the applicable milestone, assuming all other revenue recognition criteria are met.

In December 2009, we entered into a research and development collaboration agreement with KHK for the research, development and commercialization of drug delivery platforms and Dicer Substrate short-interfering RNAs ("DsiRNAs") molecules for targets, primarily in oncology (the "KHK Collaboration Agreement"). Pursuant to the KHK Collaboration Agreement, we granted KHK an exclusive license to our DsiRNA molecules and drug delivery technologies and intellectual property for two programs: KRAS and a second undisclosed oncology target. Under the KHK Collaboration Agreement, KHK is responsible for carrying out 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.

To date, we have received payments totaling $17.5 million from KHK. In November 2017, KHK provided us with notice of termination related to the non-KRAS program. Given our current development focus, including the GalXC program, we no longer consider this agreement material to our business. We did not recognize any revenue in connection with the KHK Collaboration Agreement during the years ended December 31, 2017, 2016 or 2015.

Grant 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.

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. $1.0 million of this grant was awarded in August 2016, and on September 1, 2017, we were awarded an additional grant in the amount of $1.0 million for the same project. The

Company recognized $1.1 million, $0.3 million and $0.2 million of revenue associated with the NIH grant awards for the years ended December 31, 2017, 2016 and 2015, respectively.

Grant revenue represents reimbursable subcontractor and internal costs incurred that are specifically covered by the grant, and where applicable, funding for qualifying facilities and administrative expenses.

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 preclinical development activities and our research activities under our research collaboration and license agreements. 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 and consultants;
- 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.

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.

The process of conducting preclinical studies and clinical trials necessary to obtain regulatory approval is costly and time-consuming. We, BI 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.

License agreement

In connection with our license agreement with City of Hope (“COH”), entered into in September 2007, we are required to pay an annual license maintenance fee, reimburse COH for patent costs incurred, pay an amount between $5.0 million to $10.0 million upon the achievement of certain milestones, and pay royalties on any future sales. There were no sublicense or other fees accrued as of December 31, 2017 or 2016. As of December 31, 2017, we had made total cumulative payments amounting to $5.1 million pursuant to our agreement with COH. We have recorded research and development expenses related to our agreement with COH of approximately $0.1 million during each of the years ended December 31, 2017, 2016 and 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. We may terminate the license agreement at any time upon 90 days written notice to COH. In 2017, we have elected not to make any further diligence extension payments. At this time, however, the license agreement remains in effect and discussions as to next steps are underway. Given our current development focus, including the GalXC program, we no longer consider this agreement material to our business.

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 restricted cash equivalents.

Recent Accounting Pronouncements

A summary of recent accounting pronouncements that have been adopted or are expected to be adopted by the Company is included in Note 1 to our consolidated financial statements (see Item 8 of this Annual Report on Form 10-K). Additional information regarding relevant accounting pronouncements is provided below.

Adopted in 2017

Stock-based compensation

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

Not yet adopted

Revenue recognition

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

The new revenue standard applies to all contracts with customers, and only contracts with customers are in the scope of the new revenue standard. Once a contractual arrangement is scoped into the new guidance, revenue

is recognized based on a model that includes identifying performance obligations and determining and allocating the transaction price to the performance obligations identified in the contract. Revenue is recognized as those performance obligations are satisfied. Entities have the option of using either a full retrospective or a modified retrospective approach to adopt this new guidance.

We have determined that we will apply the full retrospective method upon initial adoption of the new revenue standard. Based on our review, we do not expect that the adoption of the new revenue guidance will have a significant quantitative impact on our consolidated financial statements, although adoption of the new guidance will result in additional revenue-related disclosures in the notes to our consolidated financial statements.

Income taxes

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

Leases

In February 2016, accounting guidance related to leases was issued that will require an entity to recognize leased assets and the rights and obligations created by those leased assets on the balance sheet and to disclose key information about an entity's leasing arrangements. This guidance will become effective for us on January 1, 2019, with early adoption permitted. We expect that the adoption of this guidance will impact our consolidated financial statements and notes thereto, resulting, among other factors, from the recognition of a right of use asset and related liability related to our 2014 non-cancelable operating lease arrangement for our office and laboratory space in Cambridge, Massachusetts. As of December 31, 2017, and as presented below, our total future minimum lease obligation associated with this lease was $4.9 million, and a substantial portion of this commitment will remain outstanding at the time that we adopt the new guidance. Our evaluation of this guidance and its full impact on our consolidated financial statements will continue throughout 2018.

Statement of cash flows

In August 2016, the accounting guidance related to the statement of cash flows was amended with the intent of reducing diversity in practice as to the classification of certain transactions in the statement of cash flows. This guidance is effective for us on January 1, 2018. Additionally, in November 2016, new accounting guidance was issued related to the statement of cash flows implications related to restricted cash and cash equivalents. The guidance requires that the statement of cash flows explain the change during the period in the total of cash and cash equivalents, including amounts generally described as restricted cash or restricted cash equivalents. Entities will also be required to reconcile such total to amounts on the balance sheet and disclose the nature of the restrictions. We have concluded that transfers between restricted and unrestricted cash accounts no longer will be reported as a cash flow in our consolidated statement of cash flows beginning in 2018. We will apply this new guidance retrospectively to all periods presented in our consolidated financial statements.

Stock-based compensation

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

Results of Operations

Comparison of the years ended December 31, 2017 and 2016

The following table summarizes the results of our operations for the years ended December 31, 2017 and 2016 (in thousands):

	FOR THE YEARS ENDED DECEMBER 31,		INCREASE (DECREASE)	
	2017	2016		
Revenue from collaborative arrangement	$ 1,182	$ —	$ 1,182	—
Grant revenue	1,095	295	800	271.2%
Total revenue	2,277	295	1,982	671.9%
Expenses:				
Research and development	36,983	41,694	(4,711)	(11.3%)
General and administrative	25,881	18,349	7,532	41.0%
Total expenses	62,864	60,043	2,821	4.7%
Loss from operations	(60,587)	(59,748)	839	1.4%
Interest income	539	235	304	129.4%
Net loss	(60,048)	(59,513)	535	0.9%
Dividends on redeemable convertible preferred stock	(10,111)	—	10,111	—
Deemed dividend related to beneficial conversion feature of redeemable convertible preferred stock	(6,144)	—	6,144	—
Deemed dividend on conversion of redeemable convertible preferred stock	(3,837)	—	3,837	—
Net loss attributable to common stockholders	$ (80,140)	$ (59,513)	$20,627	34.7%

Revenue

During the year ended December 31, 2017, we recognized $1.2 million of revenue associated with the BI Agreement. This amount represents partial amortization of the $10.0 million upfront payment received from BI that is being amortized over a period of 20 months, which represents the research term over which the research and development services are provided, as well as reimbursable third-party research expenses that are billable to BI. We currently expect to recognize the remaining $9.0 million of the aforementioned non-refundable upfront payment on a straight-line basis through June 30, 2019.

The Company recognized $1.1 million and $0.3 million of revenue associated with the NIH grant awards related to cancer treatment research for the years ended December 31, 2017 and 2016, respectively, as activity ramped up in light of the availability of more recent funding.

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

Research and development expenses

The following table summarizes our research and development expenses incurred during the years ended December 31, 2017 and 2016 (in thousands):

	FOR THE YEARS ENDED DECEMBER 31,		INCREASE (DECREASE)
	2017	2016	
Direct research and development expenses	$ 16,558	$ 13,711	$ 2,847
Platform-related expenses	6,611	11,302	(4,691)
Employee-related expenses	10,590	13,159	(2,569)
Facilities, depreciation and other expenses	3,224	3,522	(298)
Total	$ 36,983	$ 41,694	$ (4,711)

Total research and development expenses decreased by $4.7 million during 2017, as compared to 2016, despite an overall increase in direct research and development expenses of $2.8 million, which was due to increased drug substance, toxicology study and manufacturing activities associated with our GalXC platform product candidates. The increase was partially offset by a decrease in comparative clinical activities related to our non-GalXC platform clinical trials, which were discontinued during 2016. Platform-related expenses decreased primarily as a result of lower spending in discovery and early development programs, which advanced in 2017 into manufacturing and clinical testing. Employee-related expenses decreased due to an overall decrease in headcount from 2016, along with a decrease in non-cash stock-based compensation costs.

We expect our overall research and development expenses to increase in 2018, as compared to 2017, as we continue spending on our development programs and related resources, including the continued advancement of our lead product candidate, DCR-PHXC, through clinical trials.

General and administrative expenses

General and administrative expenses were $25.9 million and $18.3 million for the years ended December 31, 2017 and 2016, respectively. The increase of $7.6 million was primarily due to higher costs associated with the litigation with Alnylam Pharmaceuticals, Inc. (“Alnylam”), in addition to higher salaries, benefits and other employee-related expenses.

We expect general and administrative expenses to decrease in 2018, as compared to 2017, largely because we expect to incur lower legal expenses in 2018.

Interest income

Interest income is comprised primarily of interest earned from our money market accounts and held-to-maturity investments. Interest income was $0.5 million and $0.2 million for the years ended December 31, 2017 and 2016, respectively. The increase was primarily due to higher invested amounts in 2017 primarily as a result of the receipt of net proceeds from the Private Placement, which closed in April 2017.

Dividends

Non-cash dividends of $10.1 million recorded during the year ended December 31, 2017 represent the fair value of accrued dividends on the Redeemable Convertible Preferred issued to the Preferred Holders, as well as

full accretion of share issuance costs. The fair value of the dividends on the dividend dates of June 30, 2017 and September 30, 2017 was determined using a binary lattice model that captured the intrinsic value of the underlying common stock on the declaration date and the option value of the shares and future dividends. Inputs to the lattice model included an adjusted risk rate, our common stock volatility, the underlying common stock price on the dividend date and management's judgment associated with probability simulations of various outcomes. Dividends were valued at each dividend declaration date based on various inputs and assumptions at that time.

The non-cash deemed dividend related to beneficial conversion feature of redeemable convertible preferred stock of $6.1 million for the year ended December 31, 2017 represents the value of a beneficial conversion feature ("BCF") which was recorded on the Redeemable Convertible Preferred. The BCF was recognized separately at issuance by allocating a portion of the proceeds equal to the intrinsic value of that feature to additional paid-in capital. The BCF was calculated at the commitment date, which management determined to be the date of issuance. Intrinsic value was calculated as the difference between the effective conversion price and the fair value of the Company's common stock, multiplied by the number of shares into which the issued shares of Redeemable Convertible Preferred were convertible. The BCF which was accreted in full at issuance due to the fact that the underlying shares of Redeemable Convertible Preferred were immediately convertible, and such accretion was recorded as a deemed dividend.

The non-cash deemed dividend on conversion of redeemable convertible preferred stock of $3.8 million for the year ended December 31, 2017 represents the excess fair value of common stock transferred in the conversion transaction to the Preferred Holders over the fair value of common stock issuable pursuant to the original conversion terms. This excess was recorded as a deemed dividend on conversion of the Redeemable Convertible Preferred and has been added to net loss to arrive at net loss attributable to common stockholders in our consolidated statement of operations for the year ended December 31, 2017.

As noted above, all shares of the Redeemable Convertible Preferred were converted into shares of the Company's common stock on December 18, 2017, and, as such, no additional dividends or deemed dividends will be recorded on the Redeemable Convertible Preferred in the future. No common stock dividends were recorded during the years ended December 31, 2017 or 2016.

Net loss attributable to common stockholders

Net loss attributable to common stockholders was $80.1 million and $59.5 million for the years ended December 31, 2017 and 2016, respectively. The overall increase in net loss attributable to common stockholders was due to the recording of dividends in 2017 on the Redeemable Convertible Preferred, as well as to the deemed dividends related to the BCF and upon conversion of the Redeemable Convertible Preferred, and to higher general and administrative expenses, partially offset by higher collaboration and grant revenues and lower research and development expenses.

Comparison of the years ended December 31, 2016 and 2015

The following table summarizes the results of our operations for the years ended December 31, 2016 and 2015 (in thousands):

	FOR THE YEARS ENDED DECEMBER 31,		INCREASE (DECREASE)	
	2016	2015		
Revenue	$295	$184	$111	60.3%
Expenses:				
Research and development	41,694	43,971	(2,277)	(5.2%)
General and administrative	18,349	19,240	(891)	(4.6%)
Total expenses	60,043	63,211	(3,168)	(5.0%)
Loss from operations	(59,748)	(63,027)	(3,279)	(5.2%)
Interest income	235	188	47	25.0%
Net loss attributable to common stockholders	$(59,513)	$(62,839)	$(3,326)	(5.3%)

Revenue

We recognized $0.3 and $0.2 million of revenue associated with the NIH grant awards related to cancer treatment research for the years ended December 31, 2016 and 2015, respectively.

Research and development expenses

The following table summarizes our research and development expenses incurred during the years ended December 31, 2016 and 2015 (in thousands):

	FOR THE YEARS ENDED DECEMBER 31,		INCREASE (DECREASE)
	2016	2015	
Direct research and development expenses	$ 13,711	$ 15,529	$ (1,818)
Platform-related expenses	11,302	14,066	(2,764)
Employee-related expenses	13,159	11,340	1,819
Facilities, depreciation and other expenses	3,522	3,036	486
Total	$ 41,694	$ 43,971	$ (2,277)

Research and development expenses were $41.7 million and $44.0 million for the years ended December 31, 2016, and 2015, respectively. Direct research and development expenses were $13.7 million for 2016, compared to $15.5 million for 2015. The decrease of $1.8 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 discontinued clinical trials during 2016. Platform-related expenses were $11.3 million for 2016, compared to $14.1 million for 2015. The decrease of $2.8 million 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 preclinical studies for our new GalXC platform in 2016. Employee-related expenses were $13.2 million for 2016, compared to $11.3 million for 2015. The increase of $1.8 million was primarily due to termination benefits incurred during 2016 and to additional headcount in 2016, along with an increase in stock-based compensation of $0.4 million. Facilities, depreciation and other expenses were $3.5 million for 2016, compared to $3.0 million for 2015. The increase of $0.5 million is due to increased facility costs.

General and administrative expenses

General and administrative expenses were $18.3 million and $19.2 million for the years ended December 31, 2016 and 2015, respectively. The decrease of $0.9 million was primarily due to a $0.4 million decrease in termination benefits as compared to 2015, a decrease in stock-based compensation of $0.8 million in 2016, partially offset by an increase in professional fees of $0.1 million, which in turn related primarily to legal costs incurred in connection with the Alnylam complaint.

Interest income

Interest income remained relatively stable at $0.2 million for each of the years ended December 31, 2016 and 2015 and represents interest earned from the Company's money market accounts and held-to-maturity investments.

Net loss attributable to common stockholders

Net loss attributable to common stockholders was $59.5 million and $62.8 million for the years ended December 31, 2016 and 2015, respectively. The net decrease in net loss attributable to common stockholders was predominantly due to the aforementioned decreases in research and development and general and administrative expenses.

Liquidity and Capital Resources

As of December 31, 2017, we had cash and cash equivalents and held-to-maturity investments of $113.7 million and $0.7 million in cash equivalents held in restriction.

Aggregate gross proceeds received on April 11, 2017 in connection with the closing of the Private Placement totaled $70.0 million, less related transaction costs of approximately $0.8 million, and aggregate gross proceeds received on December 18, 2017 in connection with the 2017 Offering totaled $46.0 million, less related transaction costs of approximately $3.2 million. Further, on October 27, 2017, we entered into the BI Agreement, pursuant to which, we were entitled to receive a non-refundable upfront payment of $10.0 million, less a refundable withholding tax in Germany of $1.6 million. BI paid $8.4 million to us in the fourth quarter of 2017 and remitted $1.6 million to the German tax authorities. The Company expects to receive a refund from the German tax authorities during the first half of 2018.

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 U.S. Securities and Exchange Commission ("SEC"). In December 2017, we sold an aggregate of 24,206,663 shares of our common stock, for gross proceeds of $46.0 million, pursuant to this registration statement.

Additionally, we are currently permitted to sell, from time to time through April 2, 2018: (i) up to 10,000,000 shares of our common stock; (ii) up to a maximum aggregate offering price of $50.0 million of preferred stock, debt securities, warrants or units; and (iii) up to 2,500,000 million shares of our common stock at market prices prevailing at the time of the sale pursuant to a universal shelf registration statement on Form S-3 declared effective by the SEC on April 2, 2015. As of March 7, 2018, we have sold 2,750,000 shares of our common stock pursuant to this universal shelf registration statement.

Cash flows

As of December 31, 2017, we had $113.7 million in cash and cash equivalents and held-to-maturity investments and $0.7 million in restricted cash equivalents.

The following table shows a summary of our cash flows for the years ended December 31, 2017, 2016 and 2015 (in thousands).

	FOR THE YEARS ENDED DECEMBER 31,		
	2017	2016	2015
Net cash used in operating activities	$ (45,327)	$(48,747)	$(48,799)
Net cash (used in) provided by investing activities	(19,480)	13,020	33,001
Net cash provided by financing activities	112,731	534	45,789
Increase (decrease) in cash and cash equivalents	$ 47,924	$(35,193)	$ 29,991

Operating activities

Net cash used in operating activities was $45.3 million and $48.7 million for the years ended December 31, 2017 and 2016, respectively. The $3.4 million net decrease in cash used in operating activities is due primarily to the receipt of proceeds, net of the refundable German withholding tax, from BI, as discussed above, and lower research and development expenses, partially offset by higher general and administrative expenses and other net working capital fluctuations.

Net cash used in operating activities was $48.7 million and $48.8 million for the years ended December 31, 2016 and 2015, respectively. The $0.1 million net decrease in cash used in operating activities is due primarily to a decrease in overall cash research and development expenditures of $2.5 million and a decrease in cash general and administrative expenses of $0.1 million, partially offset by a net decrease of $2.8 million in cash provided by changes in our working capital, which in turn was largely attributable to a net change in accrued expenses and other current liabilities.

Investing activities

Net cash used in investing activities for the year ended December 31, 2017 was $19.5 million, as compared to net cash provided by investing activities of $13.0 million for the year ended December 31, 2016. The increase of $32.5 million in net cash used in investing activities during 2017 relates primarily to higher purchases of held-to-maturity investments, largely following the receipt of net proceeds from the issuance of the Redeemable Convertible Preferred, partially offset by higher maturities of held-to-maturity investments. Additionally, $0.3 million of our restricted cash equivalents became unrestricted in December 2017, pursuant to the terms of our operating lease for office and laboratory space, which provided for a reduction in the amount of the letter of credit that is in place to secure our obligation.

Net cash provided by investing activities was $13.0 million and $33.0 million for the years ended December 31, 2016 and 2015, respectively. The $20.0 million decrease in net cash provided by investing activities for 2016, compared to 2015, relates primarily to a decrease in maturities of held-to-maturity investments of $21.5 million, offset slightly by a decrease in purchases of property and equipment of $0.7 million.

Financing activities

Net cash provided by financing activities was $112.7 million and $0.5 million for the years ended December 31, 2017 and 2016, respectively. The increase of $112.2 million was principally due to the receipt of $69.3 million in net proceeds from the Private Placement, as well as to the receipt of $43.2 million in net proceeds from the 2017 Offering, partially offset by lower proceeds received in connection with stock option exercises and with common stock issuances under our employee stock purchase plan.

Net cash provided by financing activities was $0.5 million and $45.8 million for the years ended December 31, 2016 and 2015, respectively. In 2015, net proceeds from a follow-on common stock offering were $45.4 million and proceeds from other issuance of common stock were $0.4 million compared to $0.6 million of proceeds from other issuance of common stock in 2016.

Funding requirements

We expect that our primary uses of capital will continue to be third-party clinical research and development services and manufacturing costs, compensation and related expenses, laboratory and related supplies, legal and other regulatory expenses, including the costs to defend the Alnylam claim of misappropriation of confidential information and trade secrets, and general overhead costs. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates and the extent to which we may enter into additional collaborations with third parties to participate in their development and commercialization, we are unable to estimate the amounts of capital outlays and operating expenditures associated with our anticipated development activities. However, based on our current operating plan, we believe that available cash, cash equivalents and held-to-maturity investments will be sufficient to fund our planned level of operations for at least the 12-month period following March 8, 2018. 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 any milestone payments under the BI Agreement;
- the terms and timing of any other collaboration, licensing and other arrangements that we may establish;
- the initiation, progress, timing and completion of preclinical studies and clinical trials for our potential product candidates;
- the number and characteristics of product candidates that we pursue;
- the outcome, timing and cost of regulatory approvals;
- delays that may be caused by changing regulatory requirements;
- the cost and timing of hiring new employees to support our continued growth;
- the costs involved in filing and prosecuting patent applications and enforcing and defending patent claims;
- the costs of filing and prosecuting intellectual property rights and enforcing and defending any intellectual property-related claims;
- the costs of responding to and defending ourselves against complaints and potential litigation, including the Alnylam complaint of misappropriation of confidential information (see Part I, Item 3—“Legal Proceedings” in this Annual Report on Form 10-K);
- the costs and timing of procuring clinical and commercial supplies for our product candidates;
- the extent to which we acquire or in-license other product candidates and technologies; and
- the extent to which we acquire or invest in other businesses, product candidates or technologies.

Until such time, if ever, we generate product revenue, we expect to finance our cash needs through a combination of public or private equity offerings, debt financings and research collaboration and license

agreements. We may be unable to raise capital or enter into such other arrangements when needed or on favorable terms, or at all. Our failure to raise capital or enter into such other arrangements in a reasonable timeframe would have a negative impact on our financial condition, and we may have to delay, reduce or terminate our research and development programs, preclinical or clinical trials, limit strategic opportunities or undergo reductions in our workforce or other corporate restructuring activities.

Please see the risk factors set forth in Part I, Item 1A—"Risk Factors" in this Annual Report on Form 10-K 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 December 31, 2017 (in thousands):

	Payments Due By Period				
	Total	Less Than 1 Year	More Than 1 Year and Less Than 3 Years	More Than 3 Years and Less Than 5 Years	More Than 5 Years
Operating lease obligation*	$4,888	$ 1,629	$ 3,259	$ —	$ —

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

We also have obligations to make future payments to licensors that become due and payable on the achievement of certain development, regulatory and commercial milestones. We have not included any such potential obligations on our consolidated balance sheet or in the table above, since the achievement and timing of these milestones were not probable or estimable as of December 31, 2017.

See also Part I, Item 3—"Legal Proceedings" in this Annual Report on Form 10-K for additional information related to litigation. We have not recorded any accruals for contingent liabilities associated with legal proceedings on our consolidated balance sheet as of December 31, 2017.

We have agreed to indemnify, under pre-determined conditions and limitations, certain counterparties for infringement of third-party intellectual property rights by us. Additionally, we have agreed to indemnify BI against any third-party damages, claims or other significant costs arising out of the lawsuit filed by Alnylam. We do not believe, based on information available, that it is probable that any material amounts will be paid under these indemnification provisions.

Off-balance Sheet Arrangements

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

Segment Reporting

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

Item 7A. ***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 December 31, 2017, we had cash and cash equivalents and held-to-maturity investments of $113.7 million. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term maturities of our cash and cash equivalents and held-to-maturity investments and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our cash and cash equivalents or held-to-maturity investments. To minimize the risk in the future, we intend to maintain our portfolio of cash and cash equivalents and held-to-maturity investments in a variety of securities, including commercial paper, money market funds and government securities.

Item 8. *Financial Statements and Supplementary Data*

DICERNA PHARMACEUTICALS, INC.
INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the shareholders and the Board of Directors of Dicerna Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Dicerna Pharmaceuticals, Inc. and subsidiaries (the "Company") as of December 31, 2017 and 2016, the related consolidated statements of operations, redeemable convertible preferred stock and stockholders' equity, and cash flows, for each of the three years in the period ended December 31, 2017, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2017, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (the "PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 8, 2018

We have served as the Company's auditor since 2008.

DICERNA PHARMACEUTICALS, INC.

Consolidated Balance Sheets
(In thousands, except share data and par value)

	DECEMBER 31,	
	2017	2016
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 68,789	$ 20,865
Held-to-maturity investments (Note 4)	44,889	25,009
Withholding tax receivable (Note 10)	1,583	—
Prepaid expenses and other current assets (Note 5)	3,297	1,952
Total current assets	118,558	47,826
NONCURRENT ASSETS:		
Property and equipment—net (Note 6)	1,512	2,234
Restricted cash equivalents (Note 13)	744	1,116
Other noncurrent assets	70	76
Total noncurrent assets	2,326	3,426
TOTAL ASSETS	$ 120,884	$ 51,252
LIABILITIES AND STOCKHOLDERS' EQUITY		
CURRENT LIABILITIES:		
Accounts payable	$ 4,920	$ 4,318
Accrued expenses and other current liabilities (Note 7)	5,726	5,726
Current portion of deferred revenue	6,000	—
Total current liabilities	16,646	10,044
Deferred revenue, net of current portion	3,000	—
TOTAL LIABILITIES	19,646	10,044
COMMITMENTS AND CONTINGENCIES (Note 13)		
STOCKHOLDERS' EQUITY:		
Preferred stock, $0.0001 par value—5,000,000 shares authorized; no shares issued or outstanding at December 31, 2017 or December 31, 2016	—	—
Common stock, $0.0001 par value—150,000,000 shares authorized; 51,644,841 and 20,594,575 shares issued and outstanding at December 31, 2017 and 2016, respectively (Note 9)	5	2
Additional paid-in capital	417,037	296,962
Accumulated deficit	(315,804)	(255,756)
Total stockholders' equity	101,238	41,208
TOTAL LIABILITIES AND STOCKHOLDERS' EQUITY	$ 120,884	$ 51,252

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

DICERNA PHARMACEUTICALS, INC.

Consolidated Statements of Operations
(In thousands, except share and per share data)

	YEARS ENDED DECEMBER 31,		
	2017	2016	2015
Revenue from collaborative arrangement (Note 10)	$ 1,182	$ —	$ —
Grant revenue (Note 10)	1,095	295	184
Total revenue	2,277	295	184
Operating expenses:			
Research and development	36,983	41,694	43,971
General and administrative	25,881	18,349	19,240
Total operating expenses	62,864	60,043	63,211
Loss from operations	(60,587)	(59,748)	(63,027)
Interest income	539	235	188
Net loss	(60,048)	(59,513)	(62,839)
Dividends on redeemable convertible preferred stock(Note 8)	(10,111)	—	—
Deemed dividend related to beneficial conversion feature of redeemable convertible preferred stock (Note 8)	(6,144)	—	—
Deemed dividend on conversion of redeemable convertible preferred stock (Note 8)	(3,837)	—	—
Net loss attributable to common stockholders	$ (80,140)	$ (59,513)	$ (62,839)
Net loss per share attributable to common stockholders—basic and diluted	$ (3.66)	$ (2.87)	$ (3.09)
Weighted average common shares outstanding—basic and diluted	21,917,415	20,719,761	20,320,628

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

DICERNA PHARMACEUTICALS, INC.

Consolidated Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity

(In thousands, except share data and par value)

	REDEEMABLE CONVERTIBLE PREFERRED STOCK $0.0001 PAR VALUE		COMMON STOCK $0.0001 PAR VALUE		ADDITIONAL PAID-IN CAPITAL	ACCUMULATED DEFICIT	TOTAL STOCKHOLDERS' EQUITY
	SHARES	AMOUNT	SHARES	AMOUNT			
BALANCE—January 1, 2015	—	—	17,786,867	3	231,741	(133,404)	98,340
Issuance of common stock from public offering, net of underwriting fees and issuance costs of $445	—	—	2,750,000	—	45,438	—	45,438
Vesting of restricted common stock	—	—	6,388	—	—	—	—
Stock-based compensation	—	—	—	—	9,732	—	9,732
Exercise of common stock options	—	—	29,506	—	149	—	149
Settlement of restricted stock for tax withholding	—	—	—	(1)	(75)	—	(76)
Sale of common stock related to employee stock purchase plan	—	—	21,814	—	278	—	278
Net loss	—	—	—	—	—	(62,839)	(62,839)
BALANCE—December 31, 2015	—	—	20,594,575	2	287,263	(196,243)	91,022
Vesting of restricted common stock	—	—	6,226	—	—	—	—
Stock-based compensation	—	—	—	—	9,165	—	9,165
Exercise of common stock options	—	—	115,699	—	396	—	396
Settlement of restricted stock for tax withholding	—	—	—	—	(27)	—	(27)
Sale of common stock related to employee stock purchase plan	—	—	36,501	—	165	—	165
Net loss	—	—	—	—	—	(59,513)	(59,513)
BALANCE—December 31, 2016	—	—	20,753,001	2	296,962	(255,756)	41,208
Issuance of redeemable convertible preferred stock, net of issuance costs of $750	700,000	69,250	—	—	—	—	—
Issuance of common stock from public offering, net of underwriting fees and issuance costs of $3,221	—	—	6,571,428	1	42,778	—	42,779
Beneficial conversion feature, redeemable convertible preferred stock	—	(6,144)	—	—	6,144	—	6,144
Deemed dividend, beneficial conversion feature, redeemable convertible preferred stock	—	6,144	—	—	(6,144)	—	(6,144)
Accretion of share issuance costs on redeemable convertible preferred stock	—	750	—	—	(750)	—	(750)
Dividends declared, redeemable convertible preferred stock	55,124	9,361	—	—	(9,361)	—	(9,361)
Conversion of redeemable convertible preferred stock	(755,124)	(79,361)	24,206,663	2	79,359	—	79,361
Vesting of restricted common stock	—	—	6,226	—	—	—	—
Stock-based compensation	—	—	—	—	7,770	—	7,770
Exercise of common stock options	—	—	24,117	—	86	—	86
Settlement of restricted stock for tax withholding	—	—	—	—	(11)	—	(11)
Sale of common stock related to employee stock purchase plan	—	—	83,406	—	204	—	204
Net loss	—	—	—	—	—	(60,048)	(60,048)
BALANCE—December 31, 2017	—	$ —	51,644,841	$ 5	$ 417,037	$ (315,804)	$ 101,238

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

DICERNA PHARMACEUTICALS, INC.

Consolidated Statements of Cash Flows
(In thousands)

	YEARS ENDED DECEMBER 31,		
	2017	2016	2015
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$ (60,048)	$ (59,513)	$ (62,839)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	7,770	9,165	9,732
Depreciation and amortization	778	840	727
Amortization of premium/(discount) on investments	(169)	73	134
Loss on disposal of property and equipment	51	—	—
Changes in operating assets and liabilities:			
Withholding tax receivable	(1,583)	—	—
Deferred revenue	9,000	—	—
Prepaid expenses and other assets	(1,341)	(414)	(177)
Accounts payable	626	1,644	1,384
Accrued expenses and other liabilities	(411)	(542)	2,240
Net cash used in operating activities	(45,327)	(48,747)	(48,799)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Change in restricted cash equivalents	372	—	264
Purchases of property and equipment	(133)	(449)	(1,134)
Maturities of held-to-maturity investments	70,000	48,500	70,000
Purchases of held-to-maturity investments	(89,719)	(35,031)	(36,129)
Net cash (used in) provided by investing activities	(19,480)	13,020	33,001
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from issuance of redeemable convertible preferred stock	70,000	—	—
Redeemable convertible preferred stock issuance costs	(750)	—	—
Proceeds from public offering of common stock, net of underwriters' commissions	43,225	—	45,438
Common stock issuance costs	(23)	—	—
Proceeds from stock option exercises and issuances under employee stock purchase plan	290	561	427
Settlement of restricted stock for tax withholding	(11)	(27)	(76)
Net cash provided by financing activities	112,731	534	45,789
INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS	47,924	(35,193)	29,991
CASH AND CASH EQUIVALENTS—Beginning of year	20,865	56,058	26,067
CASH AND CASH EQUIVALENTS—End of year	$ 68,789	$ 20,865	$ 56,058
NONCASH INVESTING ACTIVITIES:			
Property and equipment purchases included in accounts payable	$ 15	$ 53	$ 112
NONCASH FINANCING ACTIVITIES:			
Conversion of redeemable convertible preferred stock into common stock	$ 79,361	$ —	$ —
Dividends on redeemable convertible preferred stock	$ 10,111	$ —	$ —
Deemed dividend related to beneficial conversion feature of redeemable convertible preferred stock	$ 6,144	$ —	$ —
Deemed dividend on conversion of redeemable convertible preferred stock	$ 3,837	$ —	$ —
Common stock issuance costs included in accounts payable or accrued expenses	$ 423	$ —	$ —

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

DICERNA PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements
(tabular amounts in thousands, except share and per share data and where otherwise noted)

1. Description of Business and Basis of Presentation

Business

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

Basis of presentation

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP") and include the accounts of Dicerna Pharmaceuticals, Inc. and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Significant judgments and estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the revenue and expenses incurred during the reporting periods. On an ongoing basis, the Company evaluates judgments and estimates, including those related to revenue recognition, accrued expenses and in relation to, for the year ended December 31, 2017 only, the accounting associated with the Redeemable Convertible Preferred, as defined and described in Note 8. The Company bases its estimates on historical experience and on various other factors that the Company believes are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results could differ materially from those estimates.

Liquidity

Based on the Company's current operating plan and liquidity, including the receipt of $70.0 million in gross proceeds from the issuance of the Company's Redeemable Convertible Preferred, as defined and discussed in Note 8, the receipt of gross proceeds of $46.0 million in connection with the 2017 Offering, as defined and discussed in Note 9, and the receipt of upfront proceeds in connection with the BI Agreement, as defined and discussed in Note 10, management believes that available cash, cash equivalents and held-to-maturity investments will be sufficient to fund the Company's planned level of operations for at least the 12-month period following March 8, 2018, which is the date that these consolidated financial statements have been issued. Notwithstanding the availability of current liquidity, the Company's ability to fund its preclinical and clinical operations, including completion of its clinical trials, will depend on the Company's ability to raise additional capital through a combination of public or private equity offerings, debt financings, and research collaborations and license agreements. If the Company is unable to generate funding from one or more of these sources within a reasonable timeframe, it may have to delay, reduce or terminate its research and development programs, preclinical or clinical trials, limit strategic opportunities or undergo reductions in its workforce or other corporate restructuring activities.

2. Summary of Significant Accounting Policies

Cash and cash equivalents

Cash and cash equivalents include all highly liquid investments, including money market funds, maturing within 90 days from the date of purchase.

Restricted cash equivalents

Restricted cash equivalents include the balance of funds held in a money market collateral account that is restricted to secure a letter of credit for the Company's operating lease for office and laboratory space. The letter of credit is required to be maintained throughout the term of the Company's lease, which expires on November 30, 2020.

Concentrations of credit risk

Financial instruments that subject the Company to significant concentrations of credit risk consist of cash and cash equivalents, restricted cash equivalents, held-to-maturity investments and the withholding tax receivable (see Note 10). All of the Company's cash and cash equivalents, restricted cash equivalents and held-to-maturity investments are invested in money market funds or United States ("U.S.") treasury securities that management believes to be of high credit quality. The tax withholding receivable balance was current as of December 31, 2017, and Company expects to collect the receivable during the first half of 2018.

During the year ended December 31, 2017, two counterparties accounted for all of the Company's revenue, while during the year ended December 31, 2016, one counterparty accounted for all of the Company's revenue.

Property and equipment

Property and equipment are stated at cost. Major betterments are capitalized whereas expenditures for maintenance and repairs which do not improve or extend the life of the respective assets are charged to operations as incurred. Depreciation is provided using the straight-line method over the estimated useful lives, as shown below.

ASSET CATEGORY	USEFUL LIVES
Office and computer equipment	3-5 years
Laboratory equipment	5 years
Furniture and fixtures	5 years
Leasehold improvements	5 years or the remaining term of lease, if shorter

Impairment of long-lived assets

Long-lived assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of the asset may not be recoverable. When such events occur, the Company compares the carrying amounts of the assets to their undiscounted expected future cash flows. If this comparison indicates that there is an impairment, the amount of the impairment is calculated as the difference between the carrying value and fair value of the related asset. During the years ended December 31, 2017, 2016 and 2015, no impairments were recorded.

Segment and geographic information

Operating segments are defined as components (business activity from which it earns revenue and incurs expenses) of an enterprise about which discrete financial information is available and regularly reviewed by the

chief operating decision maker in deciding how to allocate resources and in assessing performance. The Company, through its Chief Executive Officer in his role as chief operating decision maker, views its operations and manages its business as one operating segment. All long-lived assets of the Company are located in the United States.

Research and development costs

Research and development costs consist of expenses incurred in performing research and development activities, including compensation and benefits for full-time research and development employees, an allocation of facility expenses, overhead expenses and other outside expenses. Research and development costs are expensed as incurred. Research and development costs that are paid in advance of performance are deferred as a prepaid expense and amortized over the service period as the services are provided.

Revenue recognition

The Company generates revenue from research collaboration and license agreements with third parties which contain multiple deliverables. The deliverables in the agreements include (a) the use of the Company's technology and (b) research and development of product candidates. Such agreements may provide for consideration to the Company in the form of up-front payments, research and development services, option payments, milestone payments and royalties.

The Company recognizes revenue for each unit of accounting when all of the following criteria have been met: (1) pervasive evidence of an arrangement exists; (2) delivery has occurred or services have been rendered and risk of loss has passed; (3) the seller's price to the buyer is fixed or determinable; and (4) collectibility is reasonably assured.

For multiple-element arrangements, the Company identifies the deliverables included in the arrangement and determines whether the individual deliverables represent separate units of accounting or whether the deliverables must be accounted for as a combined unit of accounting. This evaluation involves subjective determinations and requires management to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting if the delivered item has value to the customer on a standalone basis and, if the arrangement includes a general right of return relative to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in the Company's control. In assessing whether an item has standalone value, the Company considers factors such as the research, development, manufacturing and commercialization capabilities of the collaborator and the availability of the relevant expertise in the marketplace. In addition, the Company considers whether the collaborator can use a deliverable for its intended purpose without the receipt of the remaining deliverables, whether the value of the deliverable is dependent on the undelivered item and whether there are other vendors that could provide the undelivered items.

The Company considers whether options included in a collaborative arrangement are substantive. Options are considered substantive if, at the inception of the arrangement, the Company is at risk as to whether the collaborator will choose to exercise the option. Factors that the Company considers in evaluating whether an option is substantive include whether the optional elements are essential to the functionality of other programs nominated, whether economic factors compel the collaborator to purchase the optional elements, the cost to exercise the option, the overall objective of the arrangement and, the benefit the collaborator might obtain from the arrangement without exercising the option.

The Company recognizes arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria are satisfied for that particular unit of accounting. In the event that a deliverable does not represent a separate unit of accounting, the Company recognizes revenue from the combined unit of accounting over the Company's contractual or estimated performance period for the undelivered elements, which is typically

the term of the Company's research and development obligations. If there is no discernible pattern of performance or if objectively measurable performance measures do not exist, the Company recognizes revenue under the arrangement on a straight-line basis over the period the Company is expected to complete its performance obligations. Conversely, if the pattern of performance in which the service is provided to the customer can be determined and objectively measurable performance measures exist, then the Company recognizes revenue under the arrangement using the proportional performance method. Revenue recognized is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the straight-line method or proportional performance method, as applicable, as of each consolidated balance sheet date.

When an option is considered substantive and there is no significant incremental discount, the option is not considered a deliverable in the arrangement and no consideration is allocated to it. Conversely, when an option is not considered substantive or it is considered substantive but is priced at an incremental discount, the option is analyzed to determine if it should be combined with other deliverables in the arrangement. Options that are substantive and priced at a significant and incremental discount are further assessed to determine whether a portion of the upfront payment should be allocated to the option and other deliverables in the arrangement.

At the inception of an arrangement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment as to whether: (1) the consideration is commensurate with either the Company's performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from its performance to achieve the milestone; (2) the consideration relates solely to past performance; and (3) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. In making this assessment, management evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the particular milestone and the level of effort and investment required to achieve the milestone. There is considerable judgment involved in determining whether a milestone satisfies all of the criteria that define the milestone as substantive. Revenue from substantive milestones is recognized only upon successful achievement of the related milestone. Where milestones are not substantive, milestone payments are accounted for in the same manner as royalties, with revenue recognized upon achievement of the milestone, assuming all other revenue recognition criteria are met.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current portion of deferred revenue in the Company's consolidated balance sheet. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

Non-refundable up-front license fees under the agreement are initially recorded as deferred revenue upon receipt and are recognized as revenue over the Company's performance period as defined in the related agreement. Royalty payments are recognized as revenue based on contract terms and reported sales of licensed products, when reported sales are reliably measurable and collectibility is reasonably assured.

Research and development service revenue is recognized over the research term as the research and development services are provided. The cost of such services is reflected in research and development expenses in the period in which the expenses are incurred.

Grant revenue is recognized in the period during which the related grant research and activities are incurred and when there is reasonable assurance that (a) the Company will comply with any conditions attached to the grant and (b) the grant funding will be received. Costs associated with grants are included in research and development expenses in the Company's consolidated statement of operations.

Income taxes

The Company records deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the Company's financial statement carrying amounts and the tax basis of assets and liabilities using enacted tax rates expected to be in effect in the years in which the differences are expected to reverse. A valuation allowance is provided to reduce the net deferred tax assets to the amount that will more likely than not be realized.

The Company also assesses the probability that the positions taken or expected to be taken in its income tax returns will be sustained by taxing authorities. A "more likely than not" (more than 50 percent) recognition threshold must be met before a tax benefit can be recognized. Tax positions that are more likely than not to be sustained are reflected in the Company's consolidated financial statements. Tax positions are measured as the largest amount of tax benefit that is greater than 50 percent likely of being realized upon settlement with a taxing authority that has full knowledge of all relevant information. The difference between the benefit recognized for a position and the tax benefit claimed on a tax return is referred to as an unrecognized tax benefit. Potential interest and penalties associated with such uncertain tax positions are recorded as a component of income tax expense.

Net loss per common share attributable to common stockholders

The Company computes basic net loss per common share by dividing net loss attributable to common stockholders by the weighted average number of common shares outstanding. During periods where the Company earns net income, the Company allocates participating securities a proportional share of net income determined by dividing total weighted average participating securities by the sum of the total weighted average common shares and participating securities (the "two-class method"). The Company's vested restricted shares participate in any dividends declared by the Company and are therefore considered to be participating securities. Participating securities have the effect of diluting both basic and diluted earnings per share during periods of income. During periods where the Company incurred net loss, the Company allocates no loss to participating securities because they have no contractual obligation to share in the losses of the Company. The Company computes diluted net loss per common share after giving consideration to the dilutive effect of stock options, warrants, unvested restricted stock and Redeemable Convertible Preferred that are outstanding during the period, except where such non-participating securities would be anti-dilutive.

Comprehensive loss

The Company has no comprehensive loss items other than net loss.

Guarantees and indemnifications

The Company is not a guarantor under any agreements.

The Company leases office space under an operating lease. The Company has standard indemnification arrangements under this lease that require the Company to indemnify the landlord against losses, liabilities, and claims incurred in connection with the premises covered by the Company's lease, the Company's use of the premises, property damage or personal injury, and breach of the agreement.

Through December 31, 2017, the Company had not experienced any losses related to this indemnification obligation and no claims with respect thereto were outstanding. The Company does not expect material claims related to this indemnification obligation, and consequently, concluded that the fair value of this obligation is negligible and no related liabilities were established.

The Company has agreed to indemnify, under pre-determined conditions and limitations, certain counterparties for infringement of third-party intellectual property rights by the Company. Additionally, the Company has

agreed to indemnify Boehringer Ingelheim International GmbH ("BI") (see Note 10) against any third-party damages, claims or other significant costs arising out of the lawsuit filed by Alnylam Pharmaceuticals, Inc. ("Alnylam") (see Note 14). The Company does not believe, based on information available, that it is probable that any material amounts will be paid under these indemnification provisions.

As permitted under Delaware law, the Company indemnifies its officers, directors, and employees for certain events or occurrences while the officer or director is, or was, serving at the Company's request in such capacity. The term of the indemnification is for the officer's or director's lifetime.

Recent Accounting Pronouncements

Adopted in 2017

Stock-based compensation

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

Not yet adopted

Revenue recognition

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers (Topic 606),* which amends the guidance for accounting for revenue from contracts with customers, superseding the revenue recognition requirements in Accounting Standards Codification Topic 605, *Revenue Recognition*, and creates a new Topic 606, *Revenue from Contracts with Customers* ("Topic 606"). Topic 606 is effective for annual reporting periods beginning after December 15, 2017, with early adoption permitted. Per Topic 606, two adoption methods are allowed: retrospectively to all prior reporting periods presented, with certain practical expedients permitted, or retrospectively with the cumulative effect of initially adopting Topic 606 recognized at the date of initial application. The Company has elected to apply Topic 606 retrospectively to all prior periods presented. Based on management's review, the Company does not expect that the adoption of Topic 606 will have a significant quantitative impact on the Company's consolidated financial statements. Adoption of Topic 606 will result in additional revenue-related disclosures in the notes to the Company's consolidated financial statements.

Income taxes

In October 2016, the FASB issued ASU No. 2016-16, *Accounting for Income Taxes: Intra-Entity Asset Transfers of Assets Other than Inventory* ("ASU 2016-16"), which is part of the FASB's simplification initiative aimed at

reducing complexity in accounting standards. ASU 2016-16 eliminates the current exception that the tax effects of intra-entity asset transfers (intercompany sales) be deferred until the transferred asset is sold to a third party or otherwise recovered through use. Instead, the new guidance will require a reporting entity to recognize any tax expense from the sale of the asset in the seller's tax jurisdiction when the transfer occurs, even though the pre-tax effects of that transaction are eliminated in consolidation. Any deferred tax asset that arises in the buyer's jurisdiction would also be recognized at the time of the transfer. ASU 2016-16 will be effective for public business entities in fiscal years beginning after December 15, 2017, including interim periods within those years. Management is currently evaluating the potential impact that this guidance may have on the Company's consolidated financial statements.

Leases

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)* ("ASU 2016-02"), which amends the existing accounting standards for lease accounting, including requiring lessees to recognize most leases on their balance sheets and making targeted changes to lessor accounting. ASU 2016-02 will be effective beginning in the first quarter of 2019, with early adoption permitted. ASU 2016-02 requires a modified retrospective transition approach for all leases existing at, or entered into after, the date of initial application, with an option to use certain transition relief. Management expects that the adoption of ASU 2016-02 will result, among other factors, in the recognition of a right of use asset and related liability related to the Company's 2014 non-cancelable operating lease arrangement for office and laboratory space (see Note 13).

Statement of cash flows

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230)* ("ASU 2016-15"), a consensus of the FASB's Emerging Issues Task Force ("EITF"). ASU 2016-15 is intended to reduce diversity in practice in how certain transactions are classified in the statement of cash flows and requires companies, among other matters, to use reasonable judgment to separate cash flows. Specifically, in the absence of specific guidance, ASU 2016-15 prescribes that an entity should classify each separately identifiable cash source and use on the basis of the nature of the underlying cash flows. ASU 2016-15 is effective for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. Management does not currently expect that adoption of this guidance will have a significant impact on the Company's consolidated financial statements.

In November 2016, the FASB issued ASU No. 2016-18, *Statement of Cash Flows (Topic 230): Restricted Cash* ("ASU 2016-18"), a consensus of the FASB's EITF. ASU 2016-18 requires that the statement of cash flows explain the change during the period in the total of cash and cash equivalents, including amounts generally described as restricted cash or restricted cash equivalents. Entities will also be required to reconcile such total to amounts on the balance sheet and disclose the nature of the restrictions. By requiring that the statement of cash flows explain the change during the period in the total of cash, cash equivalents, and restricted cash, the new guidance eliminates current diversity in practice. ASU 2016-18 is effective for financial statements issued for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years, and entities must apply this new guidance retrospectively to all periods presented. The Company has concluded that, upon adoption of ASU 2016-18, transfers between restricted and unrestricted cash accounts no longer will be reported as a cash flow in the Company's consolidated statement of cash flows.

Stock-based compensation

In May 2017, the FASB issued ASU No. 2017-09, *Compensation—Stock Compensation (Topic 718): Scope of Modification Accounting* ("ASU 2017-09"), which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. Per ASU 2017-09, modification accounting is required only if the fair value, the vesting conditions, or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions, whereas under previous guidance, judgments about whether certain changes to an award are substantive may impact whether or not modification accounting is

applied in certain situations. ASU 2017-19 is effective prospectively for annual periods beginning on or after December 15, 2017, with early adoption permitted. Management will apply ASU 2017-19 to the extent that any future changes to any of the terms of outstanding stock options constitute a modification per the revised guidance.

3. Net Loss Per Share Attributable to Common Stockholders

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

	DECEMBER 31,		
	2017	2016	2015
Options to purchase common stock	6,124,096	5,099,449	4,297,300
Warrants to purchase common stock	87,901	87,901	87,901
Unvested restricted common stock	10,000	20,000	68,656
Total	6,221,997	5,207,350	4,453,857

4. Held-to-Maturity Investments

The Company invests its excess cash balances in short-term and long-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 the Company's held-to-maturity investments.

	AMORTIZED COST	GROSS UNREALIZED GAINS	GROSS UNREALIZED LOSSES	FAIR VALUE
As of December 31, 2017:				
Held-to-maturity investments				
U.S. treasury securities maturing in one year or less	$ 44,889	$ —	$ (30)	$ 44,859

	AMORTIZED COST	GROSS UNREALIZED GAINS	GROSS UNREALIZED LOSSES	FAIR VALUE
As of December 31, 2016:				
Held-to-maturity investments				
U.S. treasury securities maturing in one year or less	$ 25,009	$ —	$ (5)	$ 25,004

5. Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consists of the following:

	AS OF DECEMBER 31,	
	2017	2016
Prepaid clinical, contract research and manufacturing costs	$ 1,931	$ 1,028
Unbilled grant and research collaboration receivables	418	295
Prepaid insurance	318	352
Prepaid rent	239	—
Interest receivable and other current assets	391	277
Prepaid expenses and other current assets	$ 3,297	$ 1,952

6. Property and Equipment, Net

Property and equipment, net, consists of the following:

	AS OF DECEMBER 31,	
	2017	2016
Laboratory equipment	$ 4,410	$ 4,390
Office and computer equipment	900	864
Furniture and fixtures	479	479
Leasehold improvements	257	257
Property and equipment—at cost	6,046	5,990
Less accumulated depreciation	(4,534)	(3,756)
Property and equipment—net	$ 1,512	$ 2,234

Depreciation expense for the years ended December 31, 2017, 2016 and 2015 was $0.8 million, $0.8 million and $0.7 million, respectively.

7. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following:

	AS OF DECEMBER 31,	
	2017	2016
Accrued clinical, contract research and manufacturing costs	$ 1,860	$ 2,313
Accrued compensation and related benefits	1,987	2,113
Accrued professional fees	1,488	867
Accrued other expenses	391	433
Accrued expenses and other current liabilities	$ 5,726	$ 5,726

8. Redeemable Convertible Preferred Stock

On April 11, 2017, pursuant to a redeemable convertible preferred stock purchase agreement ("SPA") with seven institutional investors (the "Preferred Holders"), led by funds advised by Bain Capital Life Sciences L.P. ("Lead Investor"), the Company issued and sold in a private placement 700,000 shares of its newly designated Redeemable Convertible Preferred Stock, par value $0.0001 per share ("Redeemable Convertible Preferred"), at

a purchase price of $100.00 per share, for total gross proceeds of $70.0 million ("Private Placement"), less issuance costs of approximately $0.8 million. The shares of Redeemable Convertible Preferred and the shares of common stock issuable upon conversion of the Redeemable Convertible Preferred were offered and sold by the Company pursuant to an exemption from the registration requirements of the Securities Act provided by Section 4(a)(2) thereunder.

In addition to the Lead Investor, other participants in the Private Placement included affiliates of Cormorant Asset Management, LLC, Domain Associates, LLC ("Domain Associates"), EcoR1 Capital, LLC, RA Capital Management, LLC ("RA Capital") and Skyline Management LLC ("Skyline Ventures"), among others. Domain Associates, RA Capital and Skyline Ventures are entities that are affiliated or were formerly affiliated with certain members of the Company's board of directors. On March 28, 2017, in accordance with the terms of the SPA, the Company increased the size of its board of directors from eight to nine directors and approved the appointment of Adam M. Koppel, M.D., Ph.D., a managing director of the Lead Investor, as a director of the Company, effective as of the closing of the Private Placement on April 11, 2017. Dr. Koppel was reelected to the Company's board of directors by shareholder vote in June 2017.

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

Inducement and conversion

On December 13, 2017, in connection with the 2017 Offering, defined and discussed in Note 9, the Company entered into a letter agreement (the "Letter Agreement") with the Preferred Holders. Pursuant to the Letter Agreement, the Preferred Holders agreed, subject to the completion of the 2017 Offering, to optionally convert all of their shares of Redeemable Convertible Preferred, to the extent not subject to Conversion Blockers, into common stock, and consented, where applicable, to the repurchase of the residual shares of common stock that would have been issuable but for the Conversion Blockers (the "Residual Shares") for $0.0001 per share. "Conversion Blockers" refers to the beneficial ownership limitations in the Company's Certificate of Designation of the Redeemable Convertible Preferred, which included (i) a 19.99% blocker provision to comply with NASDAQ Listing Rules, (ii) if so elected by a holder, a 9.99% blocker provision that would have prohibited beneficial ownership of more than 9.99% of the outstanding shares of the Company's common stock or voting power at any time, and (iii) ownership limitations resulting from applicable regulatory restrictions.

The Letter Agreement also provided for Preferred Holders to waive and amend certain provisions in an amended and restated registration rights agreement by and among the Company and the Preferred Holders party thereto (the "Registration Rights Agreement"). In consideration for the Preferred Holders' agreeing to the optional conversion of the Redeemable Convertible Preferred and to a waiver under and certain amendments to the Registration Rights Agreement, the Company agreed to issue to the Preferred Holders pre-funded warrants (the "Pre-Funded Warrants"), exercisable in part or in whole at any time upon grant for shares of the Company's common stock at a price per share of $0.0001 per share. Each Preferred Holder was entitled to elect to receive shares of the Company's common stock in lieu of the Pre-Funded Warrants that otherwise would have been issued to such Preferred Holder subject to any applicable Conversion Blockers. Under the Letter Agreement, the number of shares allocable to each Preferred Holder was calculated based on the sum of (i) the number of shares of common stock into which the additional dividend accruals on the Redeemable Convertible Preferred that such Preferred Holders would have been entitled to receive up to and including March 31, 2018 would have been convertible, calculated immediately prior to the effectiveness of the conversion and (ii) any Residual Shares repurchased, or to be repurchased, from such Preferred Holder by the Company as described above (collectively, the "Additional Investor Shares"). The formula for the Additional Investor Shares assumes (1) a conversion price of $3.19 per share of common stock; (2) application of a dividend rate of 12% per annum from April 11, 2017 to October 27, 2017 and (3) application of a dividend rate of 8% per annum commencing from October 28, 2017 through March 31, 2018.

On December 18, 2017, the Company completed the conversion of the Redeemable Convertible Preferred and issued an aggregate of 24,206,663 shares of the Company's common stock. No Pre-Funded Warrants were issued

in connection with the conversion of the Redeemable Convertible Preferred, as all Preferred Holders opted to receive common shares in lieu of Pre-Funded Warrants, largely given the inapplicability of Conversion Blockers as of the date of conversion, immediately after which no shares of Redeemable Convertible Preferred remained outstanding.

On December 29, 2017, the Company filed with the Secretary of State of the State of Delaware a Certificate of Elimination of the Redeemable Convertible Preferred, which eliminates from the Company's Certificate of Incorporation all matters set forth in the Certificate of Designation of Redeemable Convertible Preferred Stock previously filed with the Secretary of State of the State of Delaware, which established and designated the Redeemable Convertible Preferred Stock and the rights, powers, preferences, privileges and limitations thereof.

Upon conversion of the Redeemable Convertible Preferred, the Company applied the guidance outlined in the FASB's Accounting Standard Codification ("ASC") Topic 470-20, *Debt with Conversion and Other Options* ("ASC 470-20"), which contains guidance addressing the accounting for induced conversions of convertible debt, which in turn, per the U.S. Securities and Exchange Commission's ("SEC") guidance codified in ASC Topic 260, *Earnings per Share* ("ASC 260"), should be applied also to induced conversions of convertible preferred stock.

The Company applied the guidance provided in ASC 260-10-S99-2 and compared the fair value of common stock transferred in the conversion transaction to the Preferred Holders to the fair value of common stock issuable pursuant to the original conversion terms. The resulting excess, which amounted to approximately $3.8 million, was recorded as a deemed dividend on conversion of the Redeemable Convertible Preferred and has been added to net loss to arrive at net loss attributable to common stockholders in the accompanying consolidated statement of operations for the year ended December 31, 2017.

Dividends

Each holder of Redeemable Convertible Preferred had been entitled to receive cumulative dividends on the Accrued Value, as defined below, of each share of Redeemable Convertible Preferred at an initial rate of 12% per annum, compounded quarterly and subject to two rate reductions of 4% each in connection with the occurrence of one of the agreed-upon milestone events. Entering into the BI Agreement, as defined and discussed in Note 10, constituted, per the Certificate of Designation, a milestone event for purposes of applying the first of two allowable rate reductions to dividends payable on the Redeemable Convertible Preferred. As such, the dividend rate on the Redeemable Convertible Preferred was reduced from 12% to 8%, effective on October 27, 2017. Dividends on the Redeemable Convertible Preferred accrued on the Accrued Value of each share of Redeemable Convertible Preferred until the conversion thereof, which occurred on December 18, 2017, as discussed above. "Accrued Value" meant, with respect to each share of Redeemable Convertible Preferred, the sum of (i) $100.00 plus (ii) on each quarterly dividend date, an additional amount equal to the dollar value of any dividends on a share of Redeemable Convertible Preferred which had accrued on any dividend payment date and had not previously been added to such Accrued Value.

For accounting purposes, in accordance with ASC Topic 480-10-S99, *Distinguishing Liabilities from Equity—SEC Materials* ("ASC 480-10-S99"), the Company recorded the dividends at fair value at each dividend declaration date. The fair value of the dividends was determined using a binary lattice model that captured the intrinsic value of the underlying common stock on the declaration date and the option value of the shares and future dividends.

The lattice model used to determine fair value of dividends on each dividend date through September 30, 2017, which was the last dividend date prior to conversion of the Redeemable Convertible Preferred, included the following inputs:

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

In addition to the inputs presented above, use of the lattice model applied other assumptions, including probability simulations of various outcomes largely associated with the conversion-related milestone events referred to above and with the progression of the Company's per common share price. Use of the lattice model resulted in a fair value estimate of the aggregate dividends declared on June 30, 2017 and September 30, 2017 of $1.9 million and $4.1 million, respectively.

Beneficial conversion feature

In accordance with ASC Topic 470-20, the Company recorded a beneficial conversion feature ("BCF") related to the issuance of the Redeemable Convertible Preferred. The BCF was recognized separately at issuance by allocating a portion of the proceeds equal to the intrinsic value of that feature to additional paid-in capital. The BCF was calculated at the commitment date, which management has determined to be the date of issuance. Intrinsic value is calculated as the difference between the effective conversion price and the fair value of the Company's common stock, multiplied by the number of shares into which the issued shares of Redeemable Convertible Preferred are convertible. During the year ended December 31, 2017, the Company recorded a deemed dividend charge of $6.1 million, to reflect full and immediate accretion of the discount resulting from the at-issuance BCF embedded within the Redeemable Convertible Preferred as a result of the shares being immediately convertible into shares of the Company's common stock at the option of the Preferred Holders.

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

The following table reflects the changes in Redeemable Convertible Preferred recorded during the year ended December 31, 2017.

Balance at January 1, 2017	$ —
Issuance of Redeemable Convertible Preferred	70,000
Share issuance costs	(750)
Net proceeds	69,250
Discount resulting from the BCF at issuance	(6,144)
Accretion of the discount resulting from the BCF (deemed dividend)	6,144
Dividends accrued at the stated rates	5,515
Fair value in excess of dividends accrued at the stated rates	3,846
Accretion of share issuance costs (additional dividends)	750
Balance immediately prior to conversion	79,361
Conversion of Redeemable Convertible Preferred	(79,361)
Balance at December 31, 2017	$ —

9. Common Stock and Stock Option Plan

Common stock

On December 18, 2017, the Company completed an underwritten follow-on public offering of 5,714,286 shares of common stock (the "2017 Offering"), which was made pursuant to the Company's effective registration statement on Form S-3 previously filed with the SEC. In connection with the 2017 Offering, the Company entered into an underwriting agreement (the "Underwriting Agreement") with Stifel, Nicolaus & Company, Incorporated and Evercore Group LLC as representatives of the underwriters listed in the Underwriting Agreement (collectively, the "Underwriters"), pursuant to which the Company granted to the Underwriters a 30-day option to purchase up to an additional 857,143 shares of the Company's common stock (the "Overallotment"). The Company completed the sale of 6,571,428 shares, inclusive of the Overallotment, to the Underwriters on December 18, 2017, and that sale resulted in the receipt by the Company of aggregate gross proceeds of $46.0 million, less Underwriter commissions and additional offering expenses totaling approximately $3.2 million.

Concurrent with the 2017 Offering, the Preferred Holders agreed to convert all of their shares of Redeemable Convertible Preferred, as discussed in Note 8.

Employee stock purchase plan

On January 28, 2014, the Company's stockholders approved the 2014 Employee Stock Purchase Plan ("2014 ESPP"). The 2014 ESPP permits eligible employees to enroll in an offering period comprising four six-month purchase periods. Participants may purchase shares of the Company's common stock, through payroll deductions, at a price equal to the lesser of 85% of the fair market value of the common stock on the grant date of the 24-month offering period to which the purchase period relates or 85% of the fair market value of the common stock on the purchase date of the applicable purchase period. Purchase dates under the ESPP occur on or about June 30 and December 31 of each year.

During the year ended December 31, 2017, an aggregate of 84,890 common shares were issued to employees under the 2014 ESPP at an average purchase price per share of $2.47, and as of December 31, 2017, there were 1,410,520 shares of common stock authorized for issuance pursuant to the 2014 ESPP. The 2014 ESPP provides for an automatic reserve increase equivalent to the lesser of one percent of the total number of shares of common stock issued and outstanding on December 31 of the immediately preceding calendar year and 1,000,000 shares of common stock, unless otherwise determined by the Company's board of directors.

Stock option plan

On January 14, 2014, the board of directors adopted the 2014 Performance Incentive Plan (the "2014 Plan"). The 2014 Plan authorizes the issuances of up to 1,900,000 shares of the Company's common stock, with an additional 4% of the total outstanding common shares becoming available at each year ending December 31. In June 2015, the 2014 Plan was amended to increase the replenishment percentage from 4% to 5% of outstanding common shares annually and to allow the reissuance thereunder of awards and grants that expire or are canceled, terminated, forfeited or fail to vest under previous Board-approved stock plans, as amended. The stock options for new hires generally vest 25% after 12 months, followed by ratable vesting over 36 months and expire 10 years from the grant date. Annual promotional and incentive-related grants generally vest ratably over a period of 48 months.

During 2015, the Company awarded 450,700 stock options as grants as an inducement material to individuals entering into employment with the Company ("Inducement Grants"). The Inducement Grants were approved by the Compensation Committee of the Company's board of directors and were awarded in accordance with NASDAQ Listing Rule 5635(c)(4) and outside of the 2014 Plan. As such, any shares underlying the Inducement Grants are not, upon forfeiture, cancellation or expiration, included in the pool of shares reserved for future issuance.

On March 4, 2016, the board of directors adopted a plan pursuant to which the Company may grant options to purchase common shares as an inducement to individuals to join the Company (the "2016 Inducement Plan"). The 2016 Inducement Plan allows the Company to deliver up to 250,000 shares (the "Share Limit") of its common stock to eligible persons, as defined. The Share Limit is subject to adjustment as contemplated by the provisions of the 2014 Plan. In February and May 2017, the Share Limit was adjusted to increase the pool of issuable options by 125,000 and 200,000 underlying shares, respectively. During the years ended December 31, 2017 and 2016, 400,000 and no options were awarded pursuant to the 2016 Inducement Plan, respectively. The fair value of each stock option award is estimated on the date of grant using the Black-Scholes option-pricing model that uses the assumptions noted in the table below.

Expected volatility for the Company's common stock was determined based on an average of the historical volatility of a peer group of similar companies due to limited historical volatility of the Company's own common stock. The Company also has limited stock option exercise information, and as such, the expected term of stock options granted was calculated in most cases using the simplified method, which represents the average of the contractual term of the stock option and the weighted-average vesting period of the stock option. The assumed dividend yield is based upon the Company's expectation of not paying dividends in the foreseeable future. The risk-free rate for periods within the expected life of the stock option is based upon the U.S. Treasury yield curve in effect at the time of grant.

The assumptions used in the Black-Scholes option-pricing model for all stock options granted during the years ended December 31, 2017, 2016 and 2015 are as follows:

	YEARS ENDED DECEMBER 31,		
	2017	2016	2015
Common stock price	$2.49 – $9.71	$2.94 – $9.09	$8.21 – $24.03
Expected option term (in years)	5.50 – 6.25	5.50 – 6.25	5.50 – 6.25
Expected volatility	79% – 91%	71% – 79%	67% – 71%
Risk-free interest rate	1.9% – 2.2%	1.2% – 2.0%	1.5% – 1.9%
Expected dividend yield	0.0%	0.0%	0.0%

The weighted-average grant date fair value of stock options granted during the years ended December 31, 2017, 2016 and 2015 was $2.52, $4.60 and $9.67 per share, respectively. As of December 31, 2017, there was $8.0 million of unrecognized compensation cost related to unvested employee stock options which are expected to be recognized over a weighted-average period of 2.41 years. The intrinsic value of stock options exercised was $0.1 million, $0.2 million and $0.4 million for the years ended December 31, 2017, 2016 and 2015, respectively.

A summary of stock option activity for employee and non-employee awards under the 2014 Plan, as amended, as related to the Inducement Grants and pursuant to the 2016 Inducement Plan, is presented below:

	NUMBER OF OPTIONS	WEIGHTED-AVERAGE PRICE PER SHARE	WEIGHTED-AVERAGE REMAINING CONTRACTUAL TERM (YEARS)
OUTSTANDING—January 1, 2017	5,099,449	$ 10.80	7.9
Granted	1,820,497	3.55	
Exercised	(24,117)	3.55	
Forfeited/Cancelled	(442,228)	9.02	
Expired	(329,505)	14.98	
OUTSTANDING—December 31, 2017	6,124,096	$ 8.58	7.3
EXERCISABLE—December 31, 2017	3,872,323	$ 10.39	6.5
VESTED AND EXPECTED TO VEST—December 31, 2017	5,991,642	$ 8.66	7.3

The Company has reserved a total of 516,310 shares of common stock for future issuance under the 2014 Plan and 2016 Inducement Plan as of December 31, 2017.

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

	YEARS ENDED DECEMBER 31,		
	2017	2016	2015
Research and development expenses	$ 3,536	$ 4,467	$ 4,202
General and administrative expenses	4,234	4,698	5,530
Total	$ 7,770	$ 9,165	$ 9,732

Restricted common stock and common stock warrants

In 2014, the Company issued a total of 44,000 shares of the Company's restricted common stock, of which 4,000 shares were fully vested at the grant date and the remaining shares were scheduled to vest in equal tranches over a four-year period on the anniversary date of the related grant. The fair value of these shares totaled $0.7 million at the grant date, representing a weighted-average grant date fair value per share of $16.30. As of December 31, 2017, 10,000 shares of the Company's restricted common stock were not yet vested; these shares are expected to vest in January 2018.

The following table presents the Company's common stock warrants issued and outstanding at December 31, 2017:

EXERCISE PRICE	NUMBER OF WARRANTS	REMAINING LIFE (YEARS)
$250.00	2,198	2.46
$7.00	85,703	0.48
	87,901	

All of the common stock warrants presented above have been exercisable since November 30, 2013, and there was no activity with respect to the Company's common stock warrants during the year ended December 31, 2017.

10. Revenue

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"). The initial grant covered a six-month period, with total funds available of approximately $0.2 million. In August 2016, the NCI awarded the Company an additional $1.0 million for a second phase of the Project, covering a budget period from September 1, 2016 to August 31, 2017, and on September 1, 2017, the Company was awarded an additional grant in the amount of $1.0 million for the Project, covering a budget period from September 1, 2017 to February 28, 2018. The Company recognized $1.1 million, $0.3 million and $0.2 million of revenue associated with the NIH grant awards for the years ended December 31, 2017, 2016 and 2015, respectively.

Collaborative research and license agreements

On October 27, 2017, the Company entered into a collaborative research and license agreement with BI (the "BI Agreement"), pursuant to which the Company and BI will jointly research and develop product candidates for the treatment of chronic liver disease using the GalXC platform, Dicerna's proprietary RNAi-based technology. The BI Agreement is for the development of product candidates against one target gene with an option for BI to add the development of product candidates that target a second gene. Also pursuant to the BI Agreement, Dicerna granted BI a worldwide license in connection with the research and development of the product candidates and will transfer to BI intellectual property rights of the product candidates selected by BI for clinical development and commercialization. Dicerna also may provide assistance to BI in order to help BI further develop selected product candidates. Under the terms of the BI Agreement, BI agreed to pay Dicerna a non-refundable upfront payment of $10.0 million for the first target, less a refundable withholding tax in Germany of $1.6 million. The non-refundable upfront payment was subject to a German withholding tax, which was withheld by BI and remitted to the German tax authorities in accordance with local tax law. The Company has determined that the release to the Company of the withheld funds is probable, in due consideration of the relevant provisions of the Convention Between the United States of America and the Federal Republic of Germany for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with Respect to Taxes on Income and Capital and to Certain Other Taxes ("Germany-U.S. Tax Treaty"). Therefore, the Company recorded a receivable for such amount with an offsetting amount included in deferred revenue.

During the term of the research program, BI will reimburse Dicerna the cost of materials and third-party expenses that have been included in the preclinical studies up to an agreed-upon limit. The Company is eligible to receive up to $191.0 million in potential development and commercial milestones related to the initial target. Dicerna is also eligible to receive royalty payments on potential global net sales, subject to certain adjustments, tiered from high single digits up to low double-digits. BI's option to add a second target would provide for an option fee payment and success-based development and commercialization milestones and royalty payments to Dicerna.

The deliverables at the effective date of the BI Agreement include delivery of intellectual property, conducting agreed-upon research program services and providing BI the exclusive option right to reserve additional targets. The Company concluded the performance of additional research for any additional target, if the underlying target option is exercised by BI, is not a deliverable of the agreement at inception because it is a substantive option and is not priced at a significant and incremental discount. Milestone payments that are contingent upon the Company's performance under the BI Agreement include developmental milestones totaling $39.0 million. The Company views these milestones as substantive and has excluded the amounts from allocable consideration at the outset of the arrangement. All potential commercial milestones, totaling $155.0 million, will be accounted for in the same manner as royalties and recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

The performance period is the expected period over which the services of the combined unit are performed, which spans from the contract's inception through June 30, 2019.

In December 2009, the Company entered into a research collaboration and license agreement with Kyowa Hakko Kirin Co., Ltd. ("KHK") for the Company's early generation non-GalXC Dicer Substrate RNAi technology against two targets primarily in oncology—namely, the KRAS oncogene and an additional undisclosed gene (the "KHK Collaboration Agreement"). Pursuant to the KHK Collaboration Agreement, the Company granted KHK an exclusive, worldwide, royalty-bearing and sub-licensable license to the DsiRNA and drug delivery technologies and intellectual property for certain selected DsiRNA-based compounds. Under the KHK Collaboration Agreement, KHK is responsible for activities to develop, manufacture and commercialize the selected DsiRNA-based compounds and pharmaceutical products containing such compounds.

Since contract inception, the Company has received payments totaling $17.5 million. The Company has not recognized any revenue in connection with the KHK Collaboration Agreement during the years ended December 31, 2017, 2016 or 2015. In November 2017, KHK provided the Company with notice of termination related to the non-KRAS program.

11. 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 on a recurring basis as of December 31, 2017 and 2016 are presented below:

DESCRIPTION	AS OF DECEMBER 31, 2017	LEVEL 1	LEVEL 2	LEVEL 3
Cash equivalents				
Money market fund	$ 51,441	$51,441	$ —	$ —
Held-to-maturity investments				
U.S. treasury securities	44,859	—	44,859	—
Restricted cash equivalents				
Money market fund	744	—	744	—
Total	$ 97,044	$51,441	$45,603	$ —

DESCRIPTION	AS OF DECEMBER 31, 2016	LEVEL 1	LEVEL 2	LEVEL 3
Cash equivalents				
Money market fund	$ 12,853	$12,853	$ —	$ —
Held-to-maturity investments				
U.S. treasury securities	25,004	—	25,004	—
Restricted cash equivalents				
Money market fund	1,116	—	1,116	—
Total	$ 38,973	$12,853	$26,120	$ —

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

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

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

As of December 31, 2017 and December 31, 2016, the carrying amounts of the withholding tax receivable (2017 only), accounts payable and accrued expenses approximated their estimated fair values because of the short-term nature of these financial instruments.

For the years ended December 31, 2017 and 2016, there were no transfers between Level 1 and Level 2.

12. Income Taxes

The Company has no current and no deferred income tax expense for the years ended December 31, 2017 and 2016, respectively. The Company did not record a federal income tax provision or benefit for the years ended December 31, 2017 and 2016.

The reconciliation between income taxes computed at the federal statutory income tax rate and the provision for (benefit from) income taxes is as follows:

	YEARS ENDED DECEMBER 31,		
	2017	2016	2015
Federal statutory rate	34.0%	34.0%	34.0%
Effect of:			
Impact of foreign rate differential	(17.6)	(31.4)	(12.6)
Tax reform impact	(29.6)	—	—
Change in valuation allowance	13.5	—	(24.4)
Research and development tax credit	0.6	(0.7)	0.9
Stock-based compensation	(0.8)	(0.9)	(0.9)
Other	(0.1)	(1.0)	3.0
Total	0.0%	0.0%	0.0%

The components of the Company's deferred tax assets are as follows:

	AS OF DECEMBER 31,	
	2017	2016
Deferred tax assets:		
Net operating loss carryforwards	$ 32,008	$ 36,727
Capitalized research and development costs	618	1,044
Research and development credit carryforwards	3,481	2,982
Stock compensation	6,066	7,298
Depreciation and other costs	42	(77)
Net deferred tax assets	42,215	47,974
Valuation allowance	(42,215)	(47,974)
Net deferred tax assets	$ —	$ —

On December 22, 2017, the Tax Cuts and Jobs Act (the "TCJA") was signed into law in the United States. The TCJA reduced the U.S. corporate tax rate from the 34% to 21% for tax years beginning after December 31, 2017. As a result of the newly enacted law, the Company was required to revalue all deferred tax assets and liabilities existing as of December 31, 2017 so as to reflect the reduction in the federal tax rate. This revaluation resulted in a reduction to the Company's deferred tax asset of $17.8 million, with a corresponding reduction to the Company's valuation allowance. Consequently, there was no impact on the accompanying consolidated financial statements that resulted from the reduction in the federal tax rate. Other relevant provisions of the TCJA did not have a material impact on the accompanying consolidated financial statements.

Management has evaluated the positive and negative evidence bearing upon the realizability of the Company's net deferred tax assets and has determined that it is more likely than not that the Company will not recognize the benefits of the net deferred tax assets. As a result, the Company has recorded a full valuation allowance at December 31, 2017 and 2016.

Realization of the future tax benefits is dependent on many factors, including the Company's ability to generate taxable income within the net operating loss carryforward period. Under the provisions of the Internal Revenue Code, certain substantial changes in the Company's ownership, including a sale of the Company or significant changes in ownership due to sales of equity, may have limited, or may limit in the future, the amount of net operating loss carryforwards, which could be used annually to offset future taxable income.

As of December 31, 2017, the Company had approximately $113.5 million of federal and $102.1 million of state net operating loss carryforwards. If not utilized, the federal and state net operating loss carryforwards expire starting in 2029 and 2030, respectively. Additionally, as of December 31, 2017, the Company had $2.1 million of federal and $1.3 million of Massachusetts tax credits that expire starting in 2028 and 2023, respectively.

As of December 31, 2017, the Company had $1.5 million of unrecognized tax benefits, all of which would affect income tax expense if recognized, before consideration of the Company's valuation allowance. The Company does not expect the unrecognized tax benefits to change significantly over the next 12 months. The Company recognizes both interest and penalties associated with uncertain tax positions as a component of income tax expense. As of December 31, 2017 and 2016, the Company had no accrued penalties or provisions for interest.

A reconciliation of the gross unrecognized tax benefit is as follows:

	YEARS ENDED DECEMBER 31,	
	2017	2016
Unrecognized tax benefits at the beginning of the period	$ 1,210	$ 1,430
Additions for current tax positions	243	—
Changes for previous tax positions	(2)	(220)
Unrecognized tax benefits at the end of the period	$ 1,451	$ 1,210

The Company files income tax returns in the United States, the Commonwealth of Massachusetts, Colorado and New Jersey. The tax years 2008 through 2016 remain open to examination by these jurisdictions, as carryforward attributes generated in past years may be adjusted in a future period. The Company is not currently under examination by the Internal Revenue Service or any other jurisdiction for these years. The Company has not recorded any interest or penalties for unrecognized tax benefits since its inception.

13. 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, the term of which commenced on December 1, 2014, obligates

the Company to make minimum payments totaling $9.5 million over a six-year lease term. Rent expense is recorded on a straight-line basis. As part of the lease agreement, the Company established a $1.1 million letter of credit, secured by a restricted money market account, the balance of which is presented as restricted cash equivalents at December 31, 2017 and 2016. In December 2017, pursuant to the terms of the underlying operating lease, the letter of credit amount was reduced to $0.7 million.

Rent expense was $1.6 million, $1.6 million and $1.7 million for the years ended December 31, 2017, 2016 and 2015, respectively.

Future minimum lease payments payable are as follows:

YEARS ENDING DECEMBER 31,	OPERATING LEASE
2018	$ 1,629
2019	1,678
2020*	1,581
Total	$ 4,888

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

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 ("COH"). In consideration for the right to develop, manufacture, and commercialize products based on certain of COH'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 COH for patent costs incurred, pay an amount between $5.0 million to $10.0 million upon the achievement of certain milestones, and pay royalties on any future sales. There were no sublicense or other fees accrued at December 31, 2017 and 2016. Since September 2007, the Company has made total cumulative payments of $5.1 million pursuant to its agreement with COH. The Company recorded research and development expense related to this agreement of approximately $0.1 million during each of the years ended December 31, 2017, 2016 and 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 COH. In 2017, the Company did not make any further diligence extension payments.

14. Litigation

On June 10, 2015, Alnylam filed a complaint against the Company in the Superior Court of Middlesex County, Massachusetts (the "Court"). The complaint alleges misappropriation of confidential, proprietary, and trade secret information, as well as other related claims, in connection with the Company's hiring of a number of former employees of Merck & Co., Inc. ("Merck") and its discussions with Merck regarding the acquisition of its subsidiary, Sirna Therapeutics, Inc., which was subsequently acquired by Alnylam. Alnylam seeks, among other things, damages in excess of $100.0 million, attorneys' fees, and an order permanently enjoining the Company from disclosing or using any of Alnylam's confidential information or trade secrets. The Court has set a trial date of April 23, 2018.

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

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

15. Quarterly Financial Data (Unaudited)

	FIRST QUARTER	SECOND QUARTER	THIRD QUARTER	FOURTH QUARTER	TOTAL YEAR
2017					
Total revenue	$ 133	$ 252	$ 474	$ 1,418	$ 2,277
Net loss	(14,201)	(15,225)	(15,033)	(15,589)	(60,048)
Net loss attributable to common stockholders	(14,201)	(23,991)	(19,144)	(22,804)	(80,140)
Net loss per share attributable to common stockholders—basic and diluted	$ (0.68)	$ (1.15)	$ (0.92)	$ (0.90)	$ (3.66)

	FIRST QUARTER	SECOND QUARTER	THIRD QUARTER	FOURTH QUARTER	TOTAL YEAR
2016					
Total revenue	$ —	$ —	$ 162	$ 133	$ 295
Net loss	(15,693)	(15,622)	(14,176)	(14,022)	(59,513)
Net loss attributable to common stockholders	(15,693)	(15,622)	(14,176)	(14,022)	(59,513)
Net loss per share attributable to common stockholders—basic and diluted	$ (0.76)	$ (0.75)	$ (0.68)	$ (0.68)	$ (2.87)

Net loss per share attributable to common stockholders is based on each reporting period's weighted average number of shares outstanding, which may differ on a quarter-to-quarter basis. As such, the sum of the quarterly net loss per share attributable to common stockholders amounts may not equal year-to-date net loss per share.

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Item 9. ***Changes in and Disagreements with Accountants on Accounting and Financial Disclosure***

None.

Item 9A. ***Controls and Procedures***

Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our periodic and current reports that we file under the Exchange Act, with the SEC is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our chief executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

As of the end of the period covered by this Annual Report on Form 10-K, 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, our chief executive officer and our 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.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act). Under the supervision and with the participation of our management, including our chief executive officer and chief financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2017 based on the guidelines established in Internal Control—Integrated Framework 2013 issued by the Committee of Sponsoring Organizations of the Treadway Commission. Our internal control over financial reporting includes policies and procedures that provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external reporting purposes in accordance with U.S. generally accepted accounting principles.

Based on that evaluation, management concluded that our internal control over financial reporting was effective as of December 31, 2017.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm as we are a smaller reporting company and an "emerging growth company" as of December 31, 2017, as defined in the Jumpstart Our Business Startups Act of 2012.

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 December 31, 2017, 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 a 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.

Item 9B. ***Other Information***

None.

PART III

Item 10. ***Directors, Executive Officers and Corporate Governance***

The information required by this item and not set forth below will be set forth in the definitive proxy statement (the "Proxy Statement") for our 2018 Annual Meeting of Stockholders to be filed with the SEC pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, and is incorporated herein by reference.

Information regarding our audit committee financial expert will be set forth in the Proxy Statement and is incorporated herein by reference.

We have adopted a Code of Business Conduct and Ethics applicable to all employees, including the principal executive officer, principal financial officer and principal accounting officer or controller, or persons performing similar functions. The Code of Business Conduct and Ethics is posted on our website at *www.dicerna.com*. Amendments to, and waivers from, the Code of Business Conduct and Ethics that apply to any of these officers, or persons performing similar functions, and that relate to any element of the code of ethics definition enumerated in Item 406(b) of Regulation S-K will be disclosed at the website address provided above and, to the extent required by applicable regulations, on a Current Report on Form 8-K.

Item 11. ***Executive Compensation***

The information required by this item will be set forth in the Proxy Statement and is incorporated herein by reference.

Item 12. ***Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters***

The information required by this item will be set forth in the Proxy Statement and is incorporated herein by reference.

Item 13. ***Certain Relationships and Related Transactions and Director Independence***

The information required by this item will be set forth in the Proxy Statement and is incorporated herein by reference.

Item 14. ***Principal Accountant Fees and Services***

The information required by this item will be set forth in the Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. ***Exhibits and Financial Statement Schedules***

(1) *Consolidated Financial Statements:*

The following consolidated financial statements are filed as part of this Annual Report on Form 10-K under Item 8—"Financial Statements and Supplementary Data."

(2) *Financial Statement Schedules: None*

(3) *Exhibits.*

Except as so indicated in Exhibit 32.1, the following exhibits are filed as part of, or incorporated by reference into, this Annual Report on Form 10-K.

Exhibit Number	Description of Documents
3.1(1)	Amended and Restated Certificate of Incorporation of the Company.
3.2(1)	Amended and Restated Bylaws of the Company.
3.3(11)	Certificate of Designation of Redeemable Convertible Preferred Stock.
3.4(15)	Certificate of Elimination of the Redeemable Convertible Preferred Stock, dated as of December 29, 2017.
4.1(2)	Specimen Common Stock Certificate.
4.1A(11)	Form of Redeemable Convertible Preferred Stock Certificate.
4.2(3)	Form of Warrant to Purchase Common Stock.
4.3(3)	Form of Warrant to Purchase Preferred Stock.
4.4(11)	Form of Amended and Restated Registration Rights Agreement.
4.4A(14)	Form of First Amendment to Registration Rights Agreement.
10.1(3)	2007 Employee, Director and Consultant Stock Plan, as amended (the "2007 Plan").++
10.2(3)	Form of Restricted Stock Agreement under the 2007 Plan.++
10.3(3)	Form of Incentive Stock Option Agreement under the 2007 Plan.++
10.4(3)	Form of Non-Qualified Stock Option Agreement under the 2007 Plan.++
10.5(3)	2010 Employee, Director and Consultant Equity Incentive Plan, as amended (the "2010 Plan").++
10.6(3)	Form of Stock Option Grant Notice and Stock Option Agreement under the 2010 Plan.++
10.7(3)	Form of Restricted Stock Agreement under the 2010 Plan.++

Exhibit Number	Description of Documents
10.8(2)	2014 Employee Stock Purchase Plan.++
10.9(2)	Form of Indemnification Agreement by and between the Company and each of its directors.++
10.10(3)	Letter agreement dated as of June 2, 2009, by and between the Company and David M. Madden.++
10.11(3)	Letter agreement dated as of February 28, 2011, by and between the Company and Dennis H. Langer M.D., J.D.++
10.12(4)	Lease agreement dated as of July 11, 2014, by and between the Company and King 87 CPD LLC
10.13(5)	Letter Agreement dated as of September 12, 2014, by and between the Company and Bruce Peacock.++
10.14(6)	Sales Agreement, dated as of March 12, 2015, between the Registrant and Cowen and Company, LLC.
10.15(7)	Amended and Restated 2014 Performance Incentive Plan.++
10.16(8)	Form of Incentive Stock Option Agreement under the Amended and Restated 2014 Performance Incentive Plan.++
10.17(8)	Form of Non-Qualified Stock Option Agreement under the Amended and Restated 2014 Performance Incentive Plan.++
10.18(8)	Separation Agreement dated as of December 15, 2015 by and between the Company and James E. Dentzer.++
10.19(8)	Offer Letter dated as of January 14, 2016 by and between the Company and John “Jack” Green.++
10.20(9)	Dicerna Pharmaceuticals, Inc. 2016 Inducement Plan.++
10.21(9)	Form of Dicerna Pharmaceuticals, Inc. Non-Qualified Inducement Stock Option Agreement.++
10.22(9)	Form of Non-Plan Inducement Stock Option Agreement.++
10.23(10)	Amended and Restated Employment Agreement dated as of July 8, 2016 by and between the Company and Douglas M. Fambrough, III++
10.24(10)	Amended and Restated Employment Agreement dated as of July 8, 2016 by and between the Company and Bob. D. Brown++
10.25(10)	Amended and Restated Employment Agreement dated as of July 6, 2016 by and between the Company and James B. Weissman++
10.26(10)	Amended and Restated Employment Agreement dated as of November 4, 2016 by and between the Company and John B. Green++
10.27(11)	Form of Letter Agreement by and between the Company and Adam Koppel.
10.28(11)	Form of Redeemable Convertible Preferred Stock Purchase Agreement by and among the Company and seven institutional investors led by funds advised by Bain Capital Life Sciences L.P.
10.29(12)	Employment Agreement, dated May 18, 2017, by and between the Company and Ralf Rosskamp.++
10.30(16)	Collaborative Research and License Agreement, dated October 27, 2017, by and between the Company and Boehringer Ingelheim International GmbH.†
10.31(13)	Letter Agreement entered into on December 13, 2017 by and between the Company and the holders of its redeemable convertible preferred stock.

Exhibit Number	Description of Documents
10.32(14)	Underwriting Agreement dated December 14, 2017 by and among the Company, Stifel, Nicolaus & Company, Incorporated and Evercore Group LLC.
21.1(5)	Subsidiaries of the Company.
23.1(16)	Consent of Independent Registered Accounting Firm.
24	Power of Attorney (reference is made to the signature page).
31.1(16)	Certification of the Company's principal executive officer required by Rule 13a-14(a) or Rule 15d-14(a).
31.2(16)	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.INS(16)	XBRL Report Instance Document
101.SCH(16)	XBRL Taxonomy Extension Schema Document
101.CAL(16)	XBRL Taxonomy Calculation Linkbase Document
101.LAB(16)	XBRL Taxonomy Label Linkbase Document
101.PRE(16)	XBRL Taxonomy Presentation Linkbase Document
101.DEF(16)	XBRL Taxonomy Extension Definition Linkbase Document

† Confidential treatment with respect to specific portions of this Exhibit has been requested, and such portions are omitted and have been filed separately with the Securities and Exchange Commission.

++ 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 Exchange Act , or otherwise subject to the liability of that section, nor shall such exhibit be deemed to be incorporated by reference in any registration statement or other document filed under the Securities Act, or the Exchange Act, except as otherwise stated in such filing.

(1) Incorporated by reference to the indicated exhibit in the Company's Current Report on Form 8-K filed on February 5, 2014.

(2) Incorporated by reference to the indicated exhibit in the Company's Amendment No. 3 to Registration Statement on Form S-1 (No. 333-193150) filed on January 28, 2014.

(3) Incorporated by reference to the indicated exhibit in the Company's Registration Statement on Form S-1 (No. 333-193150) filed on December 31, 2013.

(4) Incorporated by reference to the indicated exhibit in the Company's Registrant's Quarterly Report on Form 10-Q filed on November 6, 2014 (File No. 001-36281) for the quarterly period ended September 30, 2014.

(5) Incorporated by reference to the indicated exhibit in the Company's Annual Report on Form 10-K filed on March 12, 2015 (File No. 001-36281) for the annual period ended December 31, 2014.

(6) Incorporated by reference to the indicated exhibit in the Company's Registration Statement on Form S-3 (No. 333-202687) filed on March 12, 2015.

(7) Incorporated by reference to the indicated exhibit in the Company's Current Report on Form 8-K filed on July 7, 2015.

(8) Incorporated by reference to the indicated exhibit in the Company's Annual Report on Form 10-K filed on March 10, 2016 (File No. 001-36281) for the annual period ended December 31, 2015.

(9) Incorporated by reference to the indicated exhibit in the Company's Registration Statement on Form S-8 filed on March 10, 2016.

(10) Incorporated by reference to the indicated exhibit in the Company's Registrant's Quarterly Report on Form 10-Q filed on November 7, 2016 (File No. 001-36281) for the quarterly period ended September 30, 2016.

(11) Incorporated by reference to the indicated exhibit in the Company's Current Report on Form 8-K filed on March 30, 2017.
(12) Incorporated by reference to the indicated exhibit in the Company's Registrant's Quarterly Report on Form 10-Q filed on August 10, 2017 (File No. 001-36281) for the quarterly period ended June 30, 2017.
(13) Incorporated by reference to the indicated exhibit in the Company's Current Report on Form 8-K filed on December 14, 2017.
(14) Incorporated by reference to the indicated exhibit in the Company's Current Report on Form 8-K filed on December 18, 2017.
(15) Incorporated by reference to the indicated exhibit in the Company's Current Report on Form 8-K filed on December 29, 2017.
(16) Filed herewith.

Item 16. ***Form 10-K Summary***

None.

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, in Cambridge, Commonwealth of Massachusetts on March 8, 2018.

By: /s/ Douglas M. Fambrough, III
Douglas M. Fambrough, III, Ph.D.
Chief Executive Officer and Director
(Principal Executive Officer)

By: /s/ John B. Green
John B. Green
Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)

POWER OF ATTORNEY

KNOW ALL PERSON BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Douglas M. Fambrough, III, Ph.D. and John B. Green and each of them, as his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratify and confirming all that said attorneys-in-fact and agents, or any of them, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report has been signed by the following persons in the capacities and on the dates indicated:

Signature	Title	Date
/s/ Douglas M. Fambrough, III **Douglas M. Fambrough, III, Ph.D.**	Chief Executive Officer and Director (Principal Executive Officer)	March 8, 2018
/s/ John B. Green **John B. Green**	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	March 8, 2018
/s/ David M. Madden **David M. Madden**	Chairman	March 8, 2018
/s/ Martin Freed **Martin Freed, M.D.**	Director	March 8, 2018
/s/ Brian K. Halak **Brian K. Halak, Ph.D.**	Director	March 8, 2018
/s/ Stephen J. Hoffman **Stephen J. Hoffman, M.D., Ph.D.**	Director	March 8, 2018
/s/ Peter Kolchinsky **Peter Kolchinsky, Ph.D.**	Director	March 8, 2018
/s/ Adam M. Koppel **Adam M. Koppel, M.D., Ph.D.**	Director	March 8, 2018
/s/ Dennis H. Langer **Dennis H. Langer, M.D., J.D.**	Director	March 8, 2018
/s/ Bruce Peacock **Bruce Peacock**	Director	March 8, 2018

Exhibit 10.30

CONFIDENTIAL

*****Text Omitted and Filed Separately with the Securities and Exchange Commission. Confidential Treatment Requested Under 17 C.F.R. Sections 200.80(b)(4) and 240.24b-2**

Contract number: [***]

COLLABORATIVE RESEARCH AND LICENSE AGREEMENT

between

Boehringer Ingelheim International GmbH

Binger Strasse 173,
55216 Ingelheim am Rhein,
Germany
("**BOEHRINGER**")

VAT-ID-No.: DE [***]

and

Dicerna Pharmaceuticals Inc.

87 Cambridgepark Drive
Cambridge, MA 02140
USA
("**DICERNA**")

– each also hereinafter referred to as "**Party**" or collectively as "**Parties**" –

RECITALS

WHEREAS BOEHRINGER is a research-based pharmaceutical company and is interested in a research program related to DICERNA's proprietary GalXC technology which enables precise silencing of disease-driving genes in the liver, specifically targeting the hepatocyte.

WHEREAS DICERNA has experience and expertise in the Research Program (as defined below) and is willing and able to perform such research activities under the terms and conditions as set forth in this Agreement.

WHEREAS BOEHRINGER recognizes DICERNA's expertise and wishes to engage DICERNA, and DICERNA wishes to accept such engagement, to provide BOEHRINGER with Candidate Products to Targets as further described in the Research Work Plan.

NOW, THEREFORE, Parties hereto agree as follows:

1. DEFINITIONS

1.1 "**Accounting Standards**" means International Financial Reporting Standards (IFRS) or accounting principles generally accepted in the United States of America (US GAAP), or those accounting standards used in accordance with the German Handelsgesetzbuch (HGB) which standards or principles (as applicable) are currently used at the relevant time and consistently applied by the applicable Party.

1.2 "**Adverse Alnylam Litigation Impact**" shall have the meaning as defined in Section 9.2.2.

1.3 "**Affiliates**" means, with respect to a Party or Third Party, any company or business or entity controlled by, controlling, or under common control with such Party or Third Party. For the purpose, of this definition "control" means direct or indirect beneficial ownership of at least fifty percent (50 %) interest in the voting stock (or the equivalent) of such person or entity or having the right to direct, appoint or remove a majority or more of the members of its board of directors (or their equivalent), or having the power to control the general management of such person or entity, by contract, law or otherwise.

1.4 [***]

1.5 "**Alnylam Litigation**" has the meaning as defined in Section 9.2.

1.6 "**Applicable Law**" means all applicable laws, rules and regulations (including any rules, regulations, guidelines or other requirements of the Regulatory Authorities or other governmental agency) that may be in effect from time to time.

1.7 "**Background Intellectual Property**" has the meaning as defined in Section 7.1.1.

1.8 **"BOEHRINGER Product IP"** has the meaning as defined in Section 7.1.4.

1.9 "**Business Day**" means any day other than (i) Saturday, (ii) Sunday or (iii) any day on which commercial banks in Cambridge, MA USA, or Ingelheim am Rhein, Germany (as applicable) are authorized or required by law to remain closed.

1.10 "**Calendar Quarter**" means a period of three calendar months ending on 31 March, 30 June, 30 September or 31 December in any Calendar Year.

1.11 "**Calendar Year**" means a one-year period beginning on January 1st and ending on December 31st.

1.12 "**Candidate Product(s)**" means on a Target-by-Target basis, the specific molecule(s) targeting the Target and put forth by DICERNA to BOEHRINGER that such molecule(s) has/have demonstrated Target suppression in vivo as described in the Research Work Plan based on the Candidate Product Criteria.

1.13 "**Candidate Product Criteria**" means the criteria agreed by the Parties for the lead molecules and back-up molecules as set forth in the Research Work Plan.

1.14 "**Change of Control**" means (a) a transaction in which at least fifty percent (50%) of the outstanding and not publicly traded voting securities or capital stock of DICERNA are sold, conveyed or otherwise disposed; or (B) a transaction in which DICERNA (a) sells, conveys or otherwise disposes of all or substantially all of its property, assets or business; or (b) (i) merges or consolidates with any other entity; or (ii) effects any other transaction or series of transactions; in each case of clause (i) or (ii), such that the those stockholders of DICERNA which hold non-listed voting securities or capital stock of DICERNA immediately prior thereto, in aggregate, no longer own, directly or indirectly, beneficially or legally, at least fifty percent (50%) of the outstanding and not publicly traded voting securities or capital stock of the surviving entity following the closing of such merger, consolidation, other transaction or series of transactions.

1.15 "**Clinical Trial**" means any experiment in which a drug or therapy is administered or dispensed to, or used involving, one or more human subjects.

1.16 "**Combination Product**" has the meaning set forth in Section 1.47.

1.17 "**Commercially Reasonable Efforts**" means [***].

1.18 "**Confidential Information**" has the meaning as defined in Section 6.1.

1.19 "**Control**" or "**Controlled**" means, with respect to any Intellectual Property, the possession by a Party or any of its Affiliates, whether by ownership or license (other than by a license granted under this Agreement), of the ability to grant to the other Party access to such Intellectual Property, or, a license or a sublicense in, to or under such Intellectual Property as provided herein without requiring the consent of a Third Party or violating the terms of any agreement or other arrangement with any Third Party, but excluding Intellectual Property owned or controlled by a Third Party who may assume rights and obligations under this Agreement.

1.20 "**Co-Packaged Product**" means a single packaged product containing a Product and one or more other therapeutically or prophylactically active products as separate components in a co-packaged form.

1.21 "**Cover**", "**Covering**" or "**Covered**" means, with respect to a product, technology, process or method that, in the absence of ownership of or a license granted under a particular Valid Claim, the manufacture, use, offer for sale, sale or importation of such product or the practice of such technology, process or method would infringe such Valid Claim or, in the case of a Valid Claim that has not yet issued, would infringe such Valid Claim if it were to issue.

1.22 "**Default**" means, with respect to a Party, that (i) any representation or warranty of such Party set forth in this Agreement shall have been untrue in any material respect when made, or (ii) such Party shall have failed to perform any material provision set forth in this Agreement, including without limitation, the provision of Deliverables, other obligations set forth under Article 5, the license grant and assignment of rights set forth under Article 7 of this Agreement, a breach of the confidentiality and non-use obligations or publication provisions set forth under Articles 6 and 8 of this Agreement, the falsification of any reports or Results or failure to make or deposit payments when due.

1.23 "**Development Period**" means, [***].

1.24 "**Development Plan**" means the written summary prepared by BOEHRINGER of the specific development activities to be conducted by BOEHRINGER and reviewed by the Parties which includes the corresponding criteria for Product advancement and which shall be attached hereto as APPENDIX 2.

1.25 "**Deliverables**" means the providing of the defined deliverables as specified in the Research Work Plan.

1.26 "**DICERNA GalXC Technology**" means the RNAi platform targeting hepatocytes in the liver using GalNAc ligands conjugated to an extended RNAi molecule.

1.27 "**Effective Date**" means October 27, 2017.

1.28 "**Field**" means all uses, including but not limited to the use of a Product for the diagnosis, treatment, palliation or prevention of a disease or medical [***] condition in humans [***].

1.29 "**First Commercial Sale**" means, on a country-by-country and Product-by-Product basis, the first sale by BOEHRINGER, its Affiliates or Sublicensees in an arm's length transaction of such Product to a Third Party other than a Sublicensee in such country in exchange for cash (or some equivalent to which value can be assigned) after Regulatory Approval for such Product has been granted in such country.

1.30 **"FTE**" means a full time equivalent person-year based upon a total of [***] working hours per Calendar Year of scientific or technical work carried out by a duly qualified employee of DICERNA, or other person performing work on behalf of and under the supervision of DICERNA, on or directly related to the work to be conducted under the Agreement. Overtime, and work on weekends, holidays and the like shall not be counted with any multiplier (e.g. time-and-a-half or double time) toward the number of hours that are used to calculate the FTE contribution.

1.31 "**GalXC Foreground IP**" means Intellectual Property that relates exclusively to the DICERNA GalXC Technology and is generated in the course of the Research Program or in the course of research and development performed by, for or with BOEHRINGER during the Development Period provided that GalXC Foreground IP shall not include Product IP.

1.32 "**GalXC Foreground Patent Rights**" shall have the meaning set forth in Section 7.3.1.

1.33 "**Generic Competition**" means and shall be deemed to exist in a particular country in the Territory with respect to a particular Product or Combination Product in a given Calendar Quarter if in such country during such Calendar Quarter [***] the aggregate unit sales of such Generic Product or Combination Product in such country, as measured by IMS standard units sold based on data provided by IMS International, or if such data is not available, such other reliable data source as reasonably agreed upon by BOEHRINGER. If no data is commercially available, then the Parties shall agree upon a methodology for estimating the percentage unit-based market share of Generic Products in such country.

1.34 "**Generic Product**" means, with respect to a particular Product or Combination Product and a particular country, (i) any pharmaceutical product (other than the Product or Combination Product, as applicable) that contains the same active ingredient(s) in a comparable quality and quantity as such Product or Combination Product, as applicable, irrespective of its pharmaceutical form and is approved under an Abbreviated New Drug Application (ANDA) or under 505(b)(2) of the United States Federal Food, Drug and Cosmetic Act or any similar abbreviated route of approval in such country, or (ii) any biologic medicinal product (other than the Product or Combination Product, as applicable) that is a biosimilar product of such Product, and, if the Product is a component of a Combination Product, a biosimilar product of the Combination Product, and is approved under a Biological Product Licensure application submitted by any person under 42 U.S.C. § 262(k) or any similar abbreviated route of approval in such country.

1.35 "**Infringed Patent**" has the meaning set forth in Section 7.4.1.

1.36 "**Initiation**" means the first dosing of the first subject in a Clinical Trial.

1.37 "**Invention**" means any process, method, utility, formulation, composition of matter, article of manufacture, discovery or finding, or any improvement thereof, that is conceived and/or reduced to practice, whether patentable or not.

1.38 "**Invoice**" means an original invoice sent by DICERNA to BOEHRINGER with respect to any payment due hereunder, containing the information and meeting the requirements as set forth in APPENDIX 4.

1.39 "**Intellectual Property**" or "**IP**" means all Patent Rights, rights to Inventions and New Inventions, copyrights, design rights, trademarks, trade secrets, Know-How, and all other intellectual property rights (whether registered or unregistered) and all applications and rights to apply for any of them, anywhere in the world.

1.40 "**Joint Research Steering Committee**" or "**JRSC**" means the committee established to oversee the Research Work Plan during the Research Program Term.

1.41 "**Know-How**" means [***].

1.42 "**Last Product**" has the meaning set forth in Section 5.10.

1.43 "**Licensed Intellectual Property**" or "**Licensed IP**" means on a Candidate Product-by-Candidate Product basis, any and all Intellectual Property (which during the Research Program Term includes the Product IP), that is: (a) [***]. For clarity, following the Research Program Term, the Licensed IP shall in all cases exclude any Intellectual Property that would otherwise be Product IP under this Agreement.

1.44 "**Licensed Patent Rights**" has the meaning set forth in Section 7.3.2.

1.45 "**Milestone Event**" has the meaning set forth in Section 4.4.

1.46 "**Milestone Payment**" has the meaning set forth in Section 4.4.

1.47 "**Net Sales**" means, [***]

(i) [***]

(ii) [***]

(iii) [***]

(iv) [***]

(v) [***]

(vi) [***]

(vii) [***]

(viii) [***]

(ix) [***]

[***]

[***]

[***]

[***]

[***]

[***]

(i) [***]

(ii) [***]

(iii) [***]

(iv) [***]

[***]

[***].

1.48 "**New Invention**" means any Invention that is made, conceived or otherwise generated: (a) in the course of the Research Work Plan, or (b) on a Product-by-Product basis in the course of research and development performed by, for or with a Party during the Development Period on the Product and/or the relevant Target.

1.49 "**Orange Book**" has the meaning set forth in Section 7.4.6.

1.50 "**Paragraph IV Certification**" has the meaning set forth in Section 7.4.7.

1.51 "**Paragraph IV Proceeding**" has the meaning set forth in Section 7.4.7(b).

1.52 "**Patent Rights**" means any and all (i) patents, (ii) patent applications, including all provisional and non-provisional applications, foreign patent applications, patent cooperation treaty (PCT) applications, substitutions, continuations, continuations-in-part, divisions and renewals, and all patent rights granted thereon, (iii) all patents-of-addition, reissues, re-examinations and extensions or restorations by existing or future extension or restoration mechanisms, including supplementary protection certificates and equivalents thereof, (iv) inventor's certificates, letters patent, or (v) any other substantially equivalent form of government issued right substantially similar to any of the foregoing described in subsections (i) through (iv) above.

1.53 "**Patent Term Extension**" has the meaning set forth in Section 7.4.5.

1.54 "**Phase I Clinical Trial**" means a human clinical trial conducted in any country that meets the requirements of 21 CFR § 312.21(a) or the non-United States equivalent thereof. By way of example and not limitation, a Phase I Clinical Trial is usually performed as a single or multiple dose clinical study in healthy volunteers or patients to assess specific administration, distribution, metabolism, excretion (ADME), safety and tolerability, bioavailability/bioequivalence or exploratory efficacy (in the sense of demonstrating "proof-of-principle") of an investigational drug, and the emphasis in Phase I is usually on safety and tolerability and it is typically used to plan patient dosing in Phase II clinical studies. For clarity, a Phase I Clinical Trial may also represent the initial phase of a combined Phase Ib/II clinical study.

1.55 "**Phase II Clinical Trial**" means a human clinical trial conducted in any country that meets the requirements of 21 CFR § 312.21(b) or the non-United States equivalent thereof. By way of example and not limitation, a Phase II Clinical Trial is usually a well-controlled clinical study in patients designed to assess early efficacy ("proof-of-concept") or to gain dose-ranging information about an investigational drug, along with product safety data. For clarity, a Phase II Clinical Trial may also represent the second part of a combined Phase Ib/II clinical study or the initial part of a combined Phase II/III clinical study.

1.56 "**Phase III Clinical Trial**" means a human clinical trial conducted in any country that meets the requirements of 21 CFR § 312.21(c) or the non-United States equivalent thereof. By way of example and not limitation, a Phase III Clinical Trial is a large scale clinical study (usually several hundreds of patients) performed after preliminary evidence suggesting effectiveness of the drug has been obtained in Phase II clinical studies, and it is intended to gather the pivotal information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and, along with other clinical trials, to provide an adequate basis for Regulatory Approval. For clarity, a Phase III Clinical Trial may also represent the second part of a combined Phase II/III clinical study.

1.57 "**Product(s)"** means [***].

1.58 "**Product IP**" means, [***]

(a) [***]

(b) [***]

[***]

[***].

1.59 "**Product Patent Rights**" has the meaning set forth in Section 7.3.3.

1.60 "**Recognized Agent**" means any Third Party who distributes products directly to customers in countries where BOEHRINGER has no Affiliate or Sublicensee

1.61 "**Regulatory Approval**" means (a) the technical, medical and scientific licenses, registrations, authorizations and approvals (including approvals of NDAs and labeling approvals), and, if applicable, (b) any necessary pricing and/or reimbursement authorizations and approvals, of any Regulatory Authority in a country, necessary for the manufacture, use, storage, import, marketing and sale of Product in such country.

1.62 "**Regulatory Authority**" means (i) any governmental authority, notified bodies or other organization in a country or region that regulates the manufacture or sale of pharmaceutical or medicinal products or medical devices, including, without limitation, the United States Food and Drug Administration (the "**USFDA**" or "**FDA**"), and the European Medicines Agency ("**EMA**"), and any successors thereto and (ii) any other relevant bodies authorized by Applicable Law to review or otherwise exercise oversight over marketing authorization applications, other regulatory filings or regulatory approvals.

1.63 "**Reimbursement Payments**" has the meaning set forth in Section 9.2.4.

1.64 "**Research Program**" means, on a Target-by-Target basis, the discovery activities undertaken by the Parties for each Target as set forth in Article 2 and the Research Work Plan attached as APPENDIX 1.

1.65 "**Research Program Term**" has the meaning set forth in Section 2.5.

1.66 "**Research Work Plan**" means the written summary of the specific research activities to be conducted by both Parties and corresponding criteria for Candidate Product advancement attached hereto as APPENDIX 1.

1.67 "**Results**" means on a Candidate Product-by-Candidate Product and where applicable a Product-by-Product basis, all results, information, data, presentations, summaries and analyses that are generated pursuant to or prepared as a result of, or in connection with the conduct of the Research Program, including such Candidate Products as well as the composition, production and purification details thereof.

1.68 "**Royalty Term**" has the meaning set forth in Section 4.7.

1.69 "**Start of Development**" or "**SoD**" means [***].

1.70 "**Sublicensees**" means any Third Party, including [***] to whom [***] grants (i) a sublicense hereunder to further develop or commercialize Products; or (ii) otherwise grant a right to promote, distribute and sell Products, but excluding service providers, clinical research organizations, manufacturers, wholesalers and other distributors.

1.71 "**Target**" means the specific target [***] and up to one additional target selected by BOEHRINGER in accordance with Section 2.2 and cleared through an independent Third Party gatekeeper as being available for any and all uses.

1.72 "**Term**" has the meaning set forth in Section 10.1.

1.73 "**Territory**" means all of the countries in the world, and their territories and possessions.

1.74 "**Third Party**" means any person or entity other than BOEHRINGER or DICERNA or their respective Affiliates.

1.75 "**Third Party Claim**" shall have the meaning as set forth in Section 9.4.

1.76 "**Valid Claim**" means, [***].

1.77 "**VAT**" shall mean (i) any Tax imposed in compliance with the EU Council Directive of 28 November 2006 on the common system of value added tax (Directive 2006/112/EC) and (ii) any other Tax of a similar nature, whether imposed in a member state of the European Union in substitution for, or levied in addition to, such Tax referred to in paragraph (i) above, or imposed elsewhere; in all cases of (i) or (ii) above, including any additions for late payments (Säumniszuschläge) and interest (Zinsen) as well as secondary liabilities in relation thereto.

2. SUBJECT OF THE AGREEMENT

2.1 **Subject of Agreement**. The Parties agree to engage in the Research Program to develop Candidate Products directed to Targets as further described in the Research Work Plan. DICERNA will be responsible for the discovery and initial profiling of the Candidate Products, including but not limited to [***] in accordance with the Research Work Plan achieving the Candidate Product Criteria. BOEHRINGER will be responsible for selecting the Candidate Products and to move forward in accordance with the Development Plan to perform [***]. Resources shall be allocated in accordance with the Research Work Plan and Development Plan and the agreed upon estimated timelines.

2.2 **Additional Target Option**. [***]

(i) develop and agree to a Research Work Plan for the additional target,

(ii) agree to the budget for costs and expenses associated with the Research Work Plan, and

(iii) [***].

Upon completion of the activities according to Section 2.2(i) – (iii) above and after mutual agreement of the Research Work Plan and financial terms for the additional target, the additional Target Option fee pursuant to Section 4.3 below shall be due. Upon payment of the additional Target Option fee, such target shall become a Target under this Agreement. For the avoidance of doubt, it is understood and agreed by the Parties that for such additional target no upfront payment and only the Target Option fee pursuant to Section 4.3 will be paid by BOEHRINGER to DICERNA.

2.3 **DICERNA Support**. The Parties understand that it may be necessary for BOEHRINGER from time to time to seek guidance from DICERNA during the [***].

2.4 **Research Work Plan**. The Research Program shall be conducted by the Parties in accordance with the Research Work Plan attached hereto as **APPENDIX 1**. The Parties may update and amend the Research Work Plan from time to time by mutual written agreement.

2.5 **Research Program Term**. The Research Program shall be performed, on a Candidate Product-by-Candidate Product basis, during the period commencing [***] following the Effective Date and expiring upon Start of Development for such Candidate Product, unless (i) extended by BOEHRINGER and agreed to by DICERNA, or (ii) earlier terminated as provided in Article 10 of this Agreement (the "**Research Program Term**").

2.6 **Development Period**. [***].

3. REGULARITIES

3.1 **Research Program Leader**. The BOEHRINGER Research Program leader and the DICERNA Research Program leader shall be listed in APPENDIX 3 – Title: "Contact List".

The BOEHRINGER and DICERNA Research Program leader will serve as the day-to-day contact point between the Parties with respect to the Research Program and will be responsible for (i) facilitating the flow of information and otherwise promoting communication of the day-to-day work for the Research Program, (ii) coordinating all work to be conducted under the Research Program, (iii) all scientific and technical questions addressed by one Party to the other Party. The BOEHRINGER and DICERNA Research Program leaders shall conduct regular telephone conferences [***] as deemed necessary or appropriate, to exchange informal information regarding the progress of each research project under and according to the Research Work Plan for the Research Program Term.

3.2 **Change in Research Program Leader**. The Parties may change the person designated as Research Program leader upon written notice (email suffices) to the other Party, provided the new Research Program leader is suitably qualified.

3.3 **Governance**

3.3.1 **Implementation of Joint Research Committee**. The Research Program shall be conducted under the direction of a Joint Research Steering Committee. [***] Meeting dates will be defined after mutual agreement by both Parties.

3.3.2 **Responsibilities**. [***]

(a) [***]

(b) [***]

(c) [***]

[***].

3.3.3 **Decision Making Authority**. [***].

3.3.4 **Effects of Change of Control.** In case of a Change of Control and to the extent the Agreement is not terminated by BOEHRINGER pursuant to Section 10.3 below, [***].

4. PAYMENTS AND ROYALTIES

4.1 **One-time Upfront Payment**. BOEHRINGER shall pay to DICERNA, after the Effective Date and receipt by BOEHRINGER of a hardcopy original of the Agreement signed by DICERNA and within thirty (30) days following receipt of a corresponding Invoice, a one-time, non-refundable, non-reimbursable and non-creditable upfront payment of 10,000,000 US dollars (US$ ten million).

4.2 **Ancillary Expenses.** During the Research Program Term, BOEHRINGER shall reimburse DICERNA, on a non-refundable, non-reimbursable and non-creditable basis, the direct materials and third party expenses that have been agreed upon and included in the Research Work Plan up to an amount of [***] within [***] following receipt of a corresponding Invoice.

4.3 **Additional Target Option Fee.** Upon exercise of the Target Option according to Section 2.2 above, BOEHRINGER shall pay to DICERNA, a one-time non-refundable, non-reimbursable and non-creditable payment of [***].

4.4 **Milestone Payments.** BOEHRINGER shall make one-off non-refundable milestone payments (each, a "**Milestone Payment**") to DICERNA upon the occurrence of each of the milestones events (each, a "**Milestone Event**") as set forth below in this Section 4.4. [***].

4.4.1 BOEHRINGER shall pay to DICERNA a Milestone Payment in the amount of [***].

4.4.2 BOEHRINGER shall pay to DICERNA a Milestone Payment in the amount of [***].

4.4.3 BOEHRINGER shall pay to DICERNA a Milestone Payment in the amount of [***].

4.4.4 BOEHRINGER shall pay to DICERNA a Milestone Payment in the amount of [***].

4.4.5 BOEHRINGER shall pay to DICERNA a Milestone Payment in the amount of [***].

4.4.6 BOEHRINGER shall pay to DICERNA a Milestone Payment in the amount of [***].

4.4.7 BOEHRINGER shall pay to DICERNA a Milestone Payment in the amount of [***].

4.4.8 BOEHRINGER shall pay to DICERNA a Milestone Payment in the amount of [***].

4.4.9 BOEHRINGER shall pay to DICERNA a Milestone Payment in the amount of [***].

4.4.10 BOEHRINGER shall pay to DICERNA a Milestone Payment in the amount of [***].

4.4.11 BOEHRINGER shall pay to DICERNA a Milestone Payment in the amount of [***].

4.4.12 For the avoidance of doubt, each of the Milestone Payments under Sections 4.4.9 – 4.4.11 above (the "**Sales Milestone Payments**") shall be payable only one time, for the first Calendar Year in which the corresponding Milestone Event (the "**Sales Milestone Event**") is achieved, [***].

[***].

4.5 **Royalties.** As further consideration for the rights granted by DICERNA to BOEHRINGER hereunder BOEHRINGER shall pay to DICERNA the following royalties on aggregate annual Net Sales [***] in the amount set forth below.

4.5.1 [***] on the portion of the aggregate annual Net Sales [***];

4.5.2 [***] on the portion of the aggregate annual Net Sales [***];

4.5.3 [***] on the portion of the aggregate annual Net Sales [***]; and

4.5.4 [***] on the portion of the aggregate annual Net Sales [***].

4.6 **Royalty Basis**. The royalties under Section 4.5 above shall be calculated on the basis of the aggregated annual Net Sales, which in their turn shall be calculated [***]. Royalties will be payable [***] and any such payments shall be made within [***] during which the applicable Net Sales of Products occurred.

4.7 **Royalty Term**. BOEHRINGER's obligation to pay royalties shall begin, [***], and shall expire, [***] or (ii) [***] (the "**Royalty Term**"). Upon expiration of the Royalty Term for a Product [***].

4.8 **Currency Conversion**. All royalties shall be payable in full in US dollars. Any sales of Products incurred in a currency other than US dollars shall be converted to the US dollars equivalent using a rate of exchange that corresponds to the rate used by whichever of BOEHRINGER or any of its Affiliates or Sublicensees recorded such receipt or expenditure, for the respective reporting period, related to recording such Net Sales or expenses in its books and records that are maintained in accordance with Accounting Standards. If such party is not required to perform such currency conversion for its Accounting Standards reporting with respect to the applicable period, then for such period such party shall convert its amounts received and expenses incurred into US dollars using exchange rates published by the European Central Bank (ECB), Frankfurt, Germany. Any royalty amount shall be calculated based upon the US dollar equivalent calculated

4.9 **Royalty Adjustments for Generic Competition.** Royalties shall be reduced by [***] on a [***] in any Calendar Quarter in which there is Generic Competition.

4.10 **Royalty Adjustments: 3rd Party Royalties Offset.** In the event that BOEHRINGER, in order to develop and/or commercialize a Product in any country or territory, is required to make royalty payments to one or more Third Parties to obtain a license under their patent rights or technologies in the absence of which the Product could not legally be developed, manufactured or sold in such country or territory, then royalties due to DICERNA for the respective Product shall be reduced by [***] of the amount of such Third Party royalty payments.

4.11 **Royalty Adjustments: No Valid Claim**. During the applicable Royalty Term, if a Product is sold in a country or territory, and the composition of matter of such Product is not Covered by a Valid Claim of any Product Patent Right Covering the composition of matter of such Product in such country or territory at the time of sale, then the royalty rate for such Product in such country shall be reduced by [***] of the applicable rate determined pursuant to Section 4.5 above.

4.12 **Maximum Royalty Adjustments**. For clarity, in no event shall the royalties payable to DICERNA in a country or territory, as reduced by Sections 4.9 —4.11 above be reduced to less than [***] of annual Net Sales of a Product.

4.13 **Due Date Royalty Payments.** Royalty payments on Net Sales of a Product in a Calendar Quarter shall be due and payable within, as applicable, either: [***].

4.14 **Late Payments**. If BOEHRINGER fails to pay any payment due under this Agreement as provided herein on or before the date such payment is due, then such late payment will bear interest, to the extent permitted by Applicable Law, at an annual rate of [***] which applied on the due date effective for the first date on which payment was delinquent and calculated for the exact number of days in the interest period based on a year of three hundred sixty (360) days (actual/360). If the [***] is no longer published, the Parties will agree upon another internationally recognized rate which has historically been substantially equivalent to the [***] and utilize such rate retroactively to such time as the rate was no longer available.

4.15 **Taxes.** All payments under or in connection with this Agreement shall be inclusive of any Taxes and each Party shall be responsible for and shall bear, pay or set-off its own Taxes assessed by a tax or other authority except as otherwise set forth in this Agreement. "**Taxes**" shall mean all forms of preliminary or finally imposed taxation, domestic and foreign taxes, fees, levies, duties and other assessments or charges of whatever kind (including but not limited to sales, use, excise, stamp, transfer, property, value added, goods and services, withholding and franchise taxes) together with any interest, penalties or additions payable in connection with such taxes, fees, levies duties and other assessments or charges.

4.16 **Value added Tax**. All payments due to the terms of this agreement are expressed to be exclusive of value added tax (VAT) or similar indirect taxes (e.g. goods and service tax). VAT/indirect taxes shall be deducted against the payments due to the terms if legally applicable. Invoices shall be made as specified in **APPENDIX 4** – Title: "Requirements for invoice", which shall be modified in the event of a change in the applicable legal requirements.

4.17 **Billability of VAT.** The VAT amounts of invoices received by one Party are not billable to the other Party as far as the first Party has an input VAT deduction, i.e. is able to receive a refund by the competent authority. If VAT is not refundable because of legal restrictions, which are not caused by the first Party, the VAT amounts are billable to the other Party. Prior to the invoicing of the aforementioned billable amounts written approval by the other Party is mandatory. Legal restrictions which are caused by the first Party and lead to a non-billable amount shall be the following but not limited to (i) missing of a limitation period or (ii) inaccurate documents in order to receive the input VAT deduction.

4.18 **Withholding Taxes.** If the Applicable Law requires withholding by BOEHRINGER and/or its Affiliates of any taxes imposed upon DICERNA and/or its Affiliates on account of any royalties and other payments paid under this Agreement to benefit of DICERNA and/or its Affiliates, such taxes shall be retained by BOEHRINGER and/or its Affiliates as required by local law from such remittable royalty and other payment and shall be remitted by BOEHRINGER and/or its Affiliates to the proper tax authorities without undue delay on account of DICERNA and/or its Affiliates. Official receipts of payment of any retained local withholding tax shall be secured and sent by BOEHRINGER and/or its Affiliates to DICERNA and/or its Affiliates as evidence of such payment only on request by DICERNA. The Parties shall cooperate and exercise their best efforts to ensure that any withholding taxes imposed on DICERNA and/or its Affiliates are reduced as far as possible under the provisions of any relevant double tax treaty; in particular, BOEHRINGER and/or its Affiliates shall support DICERNA in DICERNA's application for an exemption certificate (*Freistellungsbescheinigung*) pursuant to sec. 50d of the German Income Tax Act (*Einkommensteuergesetz*), which provides for full exemption from German withholding tax. For the avoidance of doubt, such support does not include any tax advice from BOEHRINGER. Withholding taxes retained by BOEHRINGER and/or its Affiliates and paid to the proper German/local tax authorities as well as any refund of retained and paid local withholding taxes from the German/local tax authorities in favour of DICERNA are paid in local/German currency (Local currency/EUR). Any effect by currency conversion is for the benefit or burden of DICERNA and/or its Affiliates. The Parties agree that the principles of Section 4.8 shall apply in determining the currency conversion rate for determining the amount to be withheld, if any, from any payment. Notwithstanding the foregoing, the Parties acknowledge and agree that under Applicable Law as of the date hereof, no amounts shall be withheld in respect of royalties or other amounts required to be paid by BOEHRINGER to DICERNA and/or its Affiliates pursuant to this Agreement provided that DICERNA or, if applicable, its respective US-based Affiliates qualify for benefits under the United States-Germany double tax treaty and have received a valid exemption certificate.

4.19 **Payment Method**. All payments to be made between the Parties under this Agreement shall be made in US dollars and may be paid by wire transfer, or electronic funds transfer in immediately available funds to a bank account designated by DICERNA or BOEHRINGER, as applicable.

4.20 **Financial Audit**. [***].

4.21 **Reports and Payments.** Within [***] following the end of each Calendar Quarter, BOEHRINGER shall submit to DICERNA a written report of Net Sales of Products sold by or on behalf of BOEHRINGER, its Affiliates and Sublicensees during a Calendar Quarter in each country of the Territory in sufficient detail to permit confirmation of the accuracy of royalty payments paid. [***] Each Party will provide commercially reasonable assistance, as requested by the other Party, to comply with any applicable reporting requirements.

4.22 **No Additional Consideration**. No additional FTE payments, overhead costs or pass through costs shall be added during the Research Program Term. For clarity, during the [***], DICERNA shall provide FTE support to BOEHRINGER up to [***]. Any additional cost to be incurred by BOEHRINGER must be pre-approved by BOEHRINGER in writing.

5 OBLIGATIONS OF THE PARTIES

5.1 **Compliance with Law**. DICERNA bears the sole responsibility for and shall procure that all laboratories, rooms and equipment and the conduct of all work to be carried out by DICERNA pursuant to the Research Program, or, if applicable pursuant to the Development Plan, shall comply with the Research Work Plan and Applicable Laws. BOEHRINGER bears the sole responsibility for and shall procure that all manufacture, use, marketing, development and commercialization of any Products shall comply with all Applicable Laws.

5.2 **Candidate Products**. DICERNA shall deliver to BOEHRINGER Candidate Products that meet the Candidate Product Criteria [***].

5.3 **Candidate Product Report**. DICERNA shall provide to BOEHRINGER within [***] of the submission to BOEHRINGER of each Candidate Product a report summarizing the Results.

5.4 **Diligent Efforts**. DICERNA will use diligent efforts to carry out the Research Program, complete the Research Work Plan activities and deliver the Candidate Products within the times agreed upon and set forth in the Research Work Plan, with reasonable care and skill in accordance with all Applicable Laws and the provisions of this Agreement.

5.5 **Commercially Reasonable Efforts**. [***].

5.6 **Qualified Employees.** Each Party shall devote the efforts of suitably qualified and trained employees and research assistants capable of carrying out the activities set forth in the Research Work Plan and Development Plan to a professional standard and shall provide all necessary facilities therefore.

5.7 **Representations and Warranties of the Parties**. Each Party represents and warrants to the other Party that, as of the Effective Date:

5.7.1 it is validly existing and in good standing under the Applicable Laws of the jurisdiction of its incorporation and has the full right, power and authority to enter into this Agreement, conduct the activities allocated to it under this Agreement, grant the licenses and assign the rights under this Agreement and disclose such information and Know-How that is disclosed in performance of its obligations under this Agreement;

5.7.2 this Agreement has been duly executed by it and is legally binding upon it, enforceable in accordance with its terms, and does not conflict with any agreement, instrument or understanding, oral or written, to which it is a party or by which it may be bound, nor violate any material Applicable Law of any court, governmental body or administrative or other agency having jurisdiction over it;

5.7.3 neither it, nor any of its Affiliates are party to any agreements, oral or written, that conflict with its obligations under this Agreement;

5.7.4 neither it, nor any of its Affiliates, is a party to or otherwise bound by any oral or written contract or agreement that shall result in any person or entity obtaining any interest in, or that would give to any entity or person any right to assert any claim in or with respect to, any of BOEHRINGER's rights granted under this Agreement;

5.7.5 it has not been debarred under the US Generic Drug Enforcement Act; and

5.7.6 all of the Parties' personnel (including but not limited to all employees, agents or consultants hired by a Party and any person or entity performing work on a Party's behalf) who are involved in the Research Program or in the development of any Candidate Product or Product under this Agreement are, or when hired will be, under a written agreement whereby they have presently assigned to BOEHRINGER, or DICERNA, as applicable, any right they may have in any New Invention under this Agreement.

5.8 **Representations and Warranties of DICERNA**. DICERNA represents and warrants to BOEHRINGER that, as of the Effective Date:

5.8.1 DICERNA is the sole and exclusive owner of, or Controls, the DICERNA GalXC Technology, the Licensed Intellectual Property, and the Background Intellectual Property licensed by DICERNA to BOEHRINGER under this Agreement;

5.8.2 It has the necessary rights to the Background Intellectual Property, Licensed Intellectual Property and the DICERNA GalXC Technology licensed to BOEHRINGER under this Agreement to conduct the Research Program in the manner contemplated under the Research Work Plan;

5.8.3 Neither DICERNA nor any Affiliate have previously assigned, transferred, conveyed or otherwise encumbered its right, title and interest in and to the DICERNA GalXC Technology, the Licensed Intellectual Property, and the Background Intellectual Property in a manner that would prevent (i) DICERNA

from performing the activities under the Research Program in accordance with the Research Work Plan, and/or assigning and granting the rights to BOEHRINGER pursuant to this Agreement; (ii) BOEHRINGER or its Affiliates, subcontractors and Sublicensees from researching, developing, manufacturing and/or commercializing Products for the Target and/or from exploiting its rights and licenses granted or assigned hereunder;

5.8.4 [***], there are no claims, judgments or settlements pending with respect to the Background Intellectual Property, Licensed Intellectual Property or the DICERNA GalXC Technology licensed by DICERNA to BOEHRINGER under this Agreement and DICERNA has not received notice that any such other claims, judgments or settlements are threatened;

5.8.5 All information disclosed to BOEHRINGER by DICERNA relating to the DICERNA GalXC Technology, the DICERNA Background Intellectual Property, [***] and the materials and methods to be employed by DICERNA in the execution of the Research Work Plan and this Agreement is, at the time of disclosure, complete and accurate;

5.8.6 It is entitled to grant the licenses and assign the rights according to Article 7 below to BOEHRINGER, and that it has taken all appropriate measures (including but not limited to having appropriate agreements in place with any person or contractor involved in the Research Program) under all Applicable Laws (including the claim of any inventions made by its employees, if necessary);

5.8.7 Other than the Intellectual Property that is licensed or assigned by DICERNA to BOEHRINGER in this Agreement, DICERNA is not aware, and has not received any notice [***], of any Intellectual Property (including any Intellectual Property Controlled by a Third Party) that would be infringed, either by BOEHRINGER or by DICERNA, in the course of conducting the Research Program.

In the event any representation or warranty is determined to be untrue or inaccurate as [***].

5.9 **Debarment Notice**. Each Party agrees that it will not knowingly employ any person that has been debarred under 21 U.S.C. Section 335a to perform any services under this Agreement. If at any time a Party becomes aware that it or any person performing work under this Agreement is or will be debarred under 21 U.S.C. Section 335a, then such Party shall immediately notify the other Party of such fact.

5.10 **Exclusivity**. On a Target-by-Target basis, DICERNA shall work exclusively with BOEHRINGER and with no other party, even as to DICERNA, from the Effective Date of this Agreement until the end of the [***] with respect to such Target [***] (the "**Exclusivity Period**"), subject to Section 5.12. For the avoidance of doubt, the upfront payment according to Section 4.1 above reserves BOEHRINGER's exclusive right to the [***] Target during the applicable Exclusivity Period and the Target Option exercise fee

according to Section 4.3 above reserves BOEHRINGER's exclusive right to the additional Target during its applicable Exclusivity Period. DICERNA is prohibited from working on the Target(s) themselves or with any Third Party on the same Target(s) during the applicable Exclusivity Period.

5.11 **Evaluation Period**. On a Candidate Product-by-Candidate Product basis, BOEHRINGER shall, after receiving the reports for the Candidate Products from DICERNA for the respective Target in accordance with Section 5.3 above, further assess the Candidate Products for selection to become Products in accordance with the respective evaluation plan including reasonable timelines for selection until the decision by BOEHRINGER to initiate [***] is made for such Candidate Product, provided that any such evaluation period shall not exceed [***] (the "**Evaluation Period**"). BOEHRINGER will bear the costs of the evaluation during the Evaluation Period, including without limitation reimbursement for DICERNA FTEs that exceed [***] per annum. Any additional costs to be incurred by BOEHRINGER must be pre-approved in writing.

5.12 **End of Exclusivity**. On a Target-by-Target basis, if [***], (a) DICERNA shall be deemed to be released from the Target exclusivity under Section 5.10 above (i.e., DICERNA can work alone or with any other Third Party on the released Target), (b) such unselected Candidate Product shall no longer be deemed to be a Candidate Product and shall not be subject to this Agreement, (c) [***], and (d) such Target shall no longer be deemed to be a Target and shall not be subject to this Agreement.

5.13 **DISCLAIMER OF WARRANTIES**. EXCEPT AS OTHERWISE EXPRESSLY SET FORTH HEREIN, NEITHER PARTY MAKES ANY REPRESENTATION OR EXTENDS ANY WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, INCLUDING ALL IMPLIED WARRANTIES OF TITLE, NON-INFRINGEMENT, MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE. IN PARTICULAR, NEITHER PARTY MAKES ANY REPRESENTATION OR EXTENDS ANY WARRANTY THAT THE CANDIDATE PRODUCTS OR PRODUCT(S) WILL BE SUCCESSFULLY DEVELOPED HEREUNDER.

5.14 **Customs.**

5.14.1 Both Parties hereby agree that DICERNA will not ship any Candidate Products, without the prior written request by BOEHRINGER. BOEHRINGER will request such Candidate Products through a purchase order which will outline the specific amount and price assigned to the Candidate Product as agreed between the Parties.

5.14.2 DICERNA hereby agrees to monitor total Candidate Product synthesis/production and shipment for each Candidate Product under the Agreement on a yearly basis. DICERNA shall share such data by sending it to BOEHRINGER [***] of the beginning of each Calendar Year to document the shipments during the previous Calendar Year. Such documentation shall include shipments by Third Parties to BOEHRINGER on behalf of DICERNA.

5.14.3 To enable BOEHRINGER to perform material synthesis/production during the Development Period, DICERNA agrees to transfer the synthesis/production protocols and, in case of biological material, cell banks, of all Products to BI in accordance with a technology transfer plan agreed by the Parties [***] for a Product.

5.14.4 DICERNA agrees to collaborate with BOEHRINGER on determining the potential of DICERNA becoming an approved exporter in a country that has a reciprocal preferential trade agreement with the EU in place and therefore all Candidate Products meet preferential origin status.

5.14.5 DICERNA hereby declares that the Candidate Products referred to in this Agreement is/are originated from the home country of DICERNA and correspond and fulfill the rules of origin for preferential trade with the EU. DICERNA shall undertake to make available to the BOEHRINGER any additional documents required by the relevant customs authorities to prove this.

5.14.6 DICERNA undertakes to provide legal authorizations for the issue of preference certificates, in particular the status of the authorized exporter of Products under EU free trade agreements or a comparable status in other EU preferential agreements (for example, the status as a registered exporter in the general preferential system (GSP)) and ensure the correct exercise of the obligations resulting from the granting of the respective status

5.14.7 Solely to the extent necessary to comply with Applicable Law, following expiration or termination of this Agreement, DICERNA shall continue to reasonably support BOEHRINGER in matters related to taxes and customs compliance at BOEHRINGER's cost and expense.

6 CONFIDENTIALITY

6.1 **Confidential Information**. "**Confidential Information**" means all non-public Know-How or other information, including proprietary materials or information, disclosed by or on behalf of a Party (the "**Disclosing Party**") to the other Party or its permitted recipients (the "**Receiving Party**") prior to, on or after the Effective Date, whether or not patentable and whether or not disclosed in written, oral or electronic form or otherwise observed by the Receiving Party. It is understood and agreed by the Parties that:

6.1.1 The terms and conditions of this Agreement will be considered Confidential Information of both Parties and kept confidential by each of the Parties as set forth in this Article 6.

6.1.2 GalXC Foreground IP is Confidential Information of DICERNA.

6.1.3 The Licensed Intellectual Property (other than the Product IP and Results, the treatment of which are set forth in Section 6.1.4) shall be Confidential Information of DICERNA.

6.1.4 The Product IP and Results for a particular Candidate Product (including Product IP and Results for any Product that contains or incorporates such Candidate Product) shall be Confidential Information of both Parties during the Research Program Term and shall remain Confidential Information of both Parties unless and until there is [***], whereupon the Product IP and Results for such Candidate Product shall be and shall remain Confidential Information of BOEHRINGER. The foregoing notwithstanding, in the event that Product IP and Results are assigned back to DICERNA upon termination, abandonment or release as set forth in this Agreement, such Product IP and Results thereafter shall be Confidential Information of DICERNA.

6.2 **Non-Disclosure and Non-Use Obligation**. Except as otherwise expressly set forth herein, the Receiving Party shall keep the Confidential Information of the Disclosing Party confidential and shall not (i) disclose such Confidential Information to any person or entity without the prior written approval of the Disclosing Party, except to its employees, Affiliates, Sublicensees and contractors, all of whom will be similarly bound by the provisions of this Article 6 and for whom the Disclosing Party will be responsible, or (ii) use such Confidential Information for any purpose other than for the purposes contemplated by this Agreement.

6.3 **Return of Confidential Information**. The Receiving Party agrees and binds itself upon expiry or termination of this Agreement, to return all Confidential Information to the Disclosing Party, provided, however, one (1) copy may be retained and stored solely for the purpose of determining its obligations under this Agreement, provided that the non-disclosure and non-use obligation under this Article 6 shall continue to apply to any such copies.

6.4 **Exemption**. These confidentiality and non-use obligations do not apply to: (i) information already in the possession of the Receiving Party prior to its disclosure by the Disclosing Party as evidenced by written records, (ii) information which comes into the public domain by publication or otherwise through no breach of the obligations of confidentiality and non-use hereunder by the Receiving Party, including with respect to Section 8.1, (iii) information which has been disclosed to the Receiving Party from another source free from any obligation of confidentiality and which was not directly or indirectly obtained from the Disclosing Party, or (iv) information which is developed independently by the Receiving Party without use of or reliance upon the Confidential Information provided by the Receiving Party. For the avoidance of doubt and notwithstanding Section 6.3 (i) and (iv) above, with respect to DICERNA's obligations, the confidentiality and non-use obligations under this Article 6 shall apply to any information exclusively related to the Candidate Products.

6.5 **Permitted Disclosures**. In addition to the exceptions contained in Sections 6.2 and 6.4, the Receiving Party may disclose Confidential Information of the Disclosing Party:

6.5.1 To the extent such disclosure is required to be disclosed under law, regulation, or the order of a court of competent jurisdiction, provided, that the Receiving Party promptly notifies the Disclosing Party of such obligation beforehand and the information to be disclosed and fully cooperates with the Disclosing Party, if so requested, in maintaining the confidentiality of such information by applying for a protective order or any similar legal instrument. In any event, the compelled Receiving Party shall only disclose such Confidential Information to the extent required under Applicable Law and shall continue to treat such information as Confidential Information for all other purposes under this Agreement.

6.5.2 To the extent such disclosure is reasonably necessary to file or prosecute patent applications or regulatory filings as contemplated by this Agreement so long as there is [***] prior written notice before filing.

6.5.3 To exercise its rights and perform its obligations hereunder, provided that such disclosure is covered by terms of confidentiality and non-use at least as restrictive as those set forth herein.

6.6 **Disclosure of Agreement**. Either Party may disclose the terms of this Agreement (a) to the extent required or advisable to comply with the rules and regulations promulgated by the United States Securities and Exchange Commission or any equivalent governmental agency in any country in the Territory, (b) in connection with a prospective acquisition, merger or financing for such Party, to prospective acquirers or merger candidates or to existing or potential investors or financing sources and (c) to any sublicensee, collaborator or potential sublicensee or potential collaborator of such Party, provided that, in the case of clause (b) or (c), prior to such disclosure each such candidate, investor or financing source shall agree in writing to be bound by obligations of confidentiality and non-use no less protective of the Disclosing Party than those set forth in this Article 6.

6.7 **Encryption Technology**. The Receiving Party undertakes to protect Confidential Information (including but not limited to patent-relevant, scientific or technical information) against unauthorized access by third parties. If Confidential Information is communicated via Internet Mail, use of Internet Mail Encryption Technology is compulsory (for direct communication between the Parties, BOEHRINGER provides for a suitable technology at http://guides.boehringer-ingelheim.com free of charge).

6.8 **Use of Name and Logo**. Subject to Section 8.2, neither DICERNA nor BOEHRINGER shall use the other Party's or its Affiliates' name or logo in any label, press release or product advertising, or for any other promotional purpose, without first obtaining the other Party's written consent.

6.9 **Engaging Individuals**. Each Party undertakes that all individuals engaged in or dealing with the activities contemplated by this Agreement (including but not limited to, students, research assistants, etc.) are contractually bound to the same or at least as protective of the Disclosing Party as the obligations of confidentiality and non-use set forth in this Article 6 before being engaged or involved in such activities.

6.10 **Restrictions on Material Non-Public Information**. Each Party acknowledges that it is aware that the United States securities laws prohibit certain persons or entities who have received material, non-public information with respect to a public company from purchasing or selling securities of that public company and from communicating such information to any other person or entity under circumstances in which it is reasonably foreseeable that such Person is likely to purchase or sell such securities. Each Party acknowledges that it is familiar with the United States Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder (collectively, the "**1934 Act**"); and agrees that it will neither use, nor cause or permit any person to use, any Confidential Information in contravention of the 1934 Act, including Rule l0b-5 and Rule 14e-3 thereunder, or other applicable securities laws.

6.11 **Survival**. This Article 6 shall survive the expiry or termination of this Agreement and shall remain in full force and effect for [***] after the expiry or termination of this Agreement.

7. INTELLECTUAL PROPERTY

7.1 **Ownership**.

7.1.1 **Background IP**. With the exception of Product IP assigned to BOEHRINGER under Section 7.1.3 or assigned back to DICERNA under this Agreement, each Party shall be and shall remain the owner of any Intellectual Property that was developed [***], which a Party provides to the other Party for use in the Research Program or during the Development Period ("**Background Intellectual Property**") and this Agreement shall not affect the ownership of any Background Intellectual Property.

7.1.2 **GalXC Foreground IP**. BOEHRINGER hereby agrees and acknowledges that notwithstanding anything to the contrary in this Agreement, any and all GalXC Foreground IP shall be exclusively owned by DICERNA. [***].

7.1.3 **Product IP.** Upon [***], if applicable, DICERNA hereby, on a Target-by-Target basis, transfers and assigns, and agrees to transfer and assign, effective [***], to BOEHRINGER DICERNA's [***] It is understood by the Parties that in the event BOEHRINGER decides to ultimately and completely abandon the development of the Product and notifies DICERNA of the same, BOEHRINGER hereby, upon such notification, transfers and assigns, and agrees to transfer and assign, effective [***], to DICERNA all of [***] and the provisions of Sections 7.3 (other than Section 7.3.4) and 7.4 of this Agreement shall no longer apply with respect to such Product IP.

7.1.4 **BOEHRINGER Product IP.** It is understood and agreed by the Parties that, on a Candidate Product-by-Candidate Product basis, any Intellectual Property (including but not limited to Patent Rights) which relates specifically to [***] ("**BOEHRINGER Product IP**") shall be and shall remain the sole and exclusive property of BOEHRINGER, even if BOEHRINGER decides to ultimately and completely abandon development of the relevant Product(s).

7.1.5 **Disclosure of Inventions by Personnel.** [***].

7.1.6 **Execution and Assignment**. Each Party further agrees that it shall, upon request of the other Party and at the other Party's cost and expense, [***] in order to confirm assignment and convey to the requesting Party the sole and exclusive right, title and interest in and to such Intellectual Property and/or any applications for intellectual property rights (including without limitation Patent Rights) thereon.

7.2 **Licenses**

7.2.1 **Research License**. Each Party grants the other Party and its Affiliates during the Research Program Term and Development Period, a royalty free, non-exclusive, worldwide license to use its Background Intellectual Property only for the purpose of carrying out the Research Program and the Development Plan.

7.2.2 **Candidate Product License**. During the Research Program Term and Development Period, DICERNA shall grant and hereby grants to BOEHRINGER and its Affiliates, [***] a [***] license [***] under DICERNA's rights in the Results, the Licensed Intellectual Property, and the Product IP (to the extent that such Product IP has not been already assigned to BOEHRINGER pursuant to Section 7.1.3 and until such assignment of such Product IP to BOEHRINGER). The license granted under this Section 7.2.2 shall be and is solely limited to the carrying out of [***].

7.2.3 **Product License**. DICERNA shall grant and hereby grants to BOEHRINGER and its Affiliates, on a Product-by-Product basis, effective upon [***] for such Product, a [***] license, [***] under DICERNA's rights (i) in the Results and (ii) the Licensed Intellectual Property to [***].

7.2.4 **Sublicensing.** Neither Party may grant any sublicense to use the other Party's Background Intellectual Property under Section 7.2.1, except that [***].

7.2.5 **No Implied Licenses**. Except as expressly provided in this Agreement, neither Party shall be deemed to have granted the other Party any license or other right with respect to any Intellectual Property of such Party.

7.3 **Patent Prosecution and Maintenance.**

7.3.1 **GalXC Foreground IP.** DICERNA shall prosecute, defend and maintain Patent Rights which are part of the GalXC Foreground IP ("**GalXC Foreground Patent Rights**"), and shall be responsible and pay all future costs and expenses incurred for the preparation, filing, prosecution, issuance and maintenance of such Patent Rights. DICERNA shall [***] inform BOEHRINGER regarding the filing, prosecution, defense and maintenance of the GalXC Foreground Patent Rights, and shall afford BOEHRINGER a [***] to review and comment on[***]for any GalXC Foreground Patent Right [***] in connection with any GalXC Foreground Patent Right.

7.3.2 **Licensed Patent Rights.** DICERNA shall have the right (but not the obligation) to prosecute, defend and maintain Patent Rights which are part of the Licensed IP ("**Licensed Patent Rights**"), and shall be responsible and pay all future costs and expenses incurred for the preparation, filing, prosecution, issuance, defense and maintenance of the Licensed Patent Rights in the Territory.

7.3.3 **Product Patent Rights**. Notwithstanding Section 7.3.2, during the Research Program Term, with respect to the Patent Rights constituting or claiming Product IP ("**Product Patent Rights**"), DICERNA shall:

(a) [***]

(b) [***]

(c) [***]

[***]

[***]

[***].

7.3.4 **Reversion**. Upon assignment of Product IP back to DICERNA as provided in this Agreement, DICERNA shall have the right (but not the obligation) to prosecute, defend and maintain the Product Patent Rights in such Product IP (which, upon assignment back to DICERNA, shall no longer be deemed to be Product Patent Rights under this Agreement), and DICERNA shall be responsible and pay all future costs and expenses incurred for the preparation, filing, prosecution, issuance and maintenance of such Product Patent Rights.

7.4 **Patent Enforcement.**

7.4.1 **Third Party Infringement.** During the Term, the Parties shall [***] inform each other [***] of any [***] infringement by any Third Party of a Product Patent Right or Licensed Patent Right ("**Infringed Patent**") [***].

7.4.2 **Product IP Infringement.** During the Term, where the Infringed Patent is a Product Patent Right [***].

7.4.3 **Third Party Patent Challenges.** The provisions of Section 7.4.2 (Product IP Infringement) shall additionally apply in the case of any objection, opposition or challenge, by a Third Party, to a Product Patent Right [***].

7.4.4 **Recoveries.** Any amount recovered in any action under this Section 7.4, including any amount recovered in any settlement of such action, shall be for the benefit of BOEHRINGER; provided, however, that any such proceeds actually received by BOEHRINGER shall, on a Product-by-Product basis, be deemed to be gross sales of such Product and that DICERNA shall receive royalties on such imputed gross sales pursuant to Section 4.5. BOEHRINGER shall be entitled to deduct from such gross sales, on a Product-by-Product basis, the costs and expenses actually borne by and not reimbursed to BOEHRINGER in relation to the enforcement and/or defense of the Infringed Patent against Third Parties from the Net Sales of such Product (and where such costs and expenses exceed the proceeds, to carry forward the respective non-deductible costs).

7.4.5 **Patent Term Extensions.** [***].

7.4.6 **Patent Linkage.** [***].

7.4.7 **Enforcement of Listed Patents.** [***]

(a) [***]

(b) [***].

8. PUBLICATIONS

8.1 **Publication Rights**. [***].

8.2 **Press Release**. The Parties may issue a press release following the execution of this Agreement describing the nature of the collaboration between BOEHRINGER and DICERNA in the form as mutually agreed to by the Parties.

9. INDEMNIFICATION AND LIABILITY

9.1. **Indemnification by DICERNA.** [***] DICERNA shall indemnify, defend, and hold harmless BOEHRINGER, and its Affiliates, and their respective officers, directors, employees, licensees, and their respective successors, heirs and assigns and representatives (the "**BOEHRINGER Indemnitees**"), from and against any and all damages, losses, suits, proceedings, liabilities, costs (including without limitation reasonable legal expenses, costs of litigation and reasonable attorney's fees) or judgments, whether for money or equitable relief, of any kind ("**Damages**") resulting from Third Party Claims brought against a BOHERINGER Indemnitee, to the extent directly or indirectly arising out of or relating to (i) the negligence, recklessness or wrongful intentional acts or omissions of DICERNA, its Affiliates and/or subcontractors and its respective officers, directors, or employees in connection with DICERNA's performance of its obligations under this Agreement, (ii) any breach by DICERNA of any obligation, representation, warranty or covenant set forth in this Agreement, and (iii) the failure to comply with any Applicable Laws by DICERNA, its Affiliates, or any of its subcontractors, except in any such case for Damages to the extent reasonably attributable to any BOEHRINGER Indemnitee with respect to any matter for which BOEHRINGER is liable to indemnify DICERNA pursuant to Section 9.3.

9.2. **Alnylam Litigation**. DICERNA is (i) the defendant in a trade secret misappropriation lawsuit brought by Alnylam against DICERNA and (ii) the plaintiff in a lawsuit against Alnylam brought in Federal Court (Alnylam Pharmaceuticals, Inc. v. Dicerna Pharmaceuticals, Inc., No. 15-cv-4126-H and Dicerna Pharmaceuticals, Inc. v. Alnylam Pharmaceuticals, Inc., docket number 1:17-cv-11466-DLC), (collectively, the "**Alnylam Litigation**"). With regard to the Alnylam Litigation, the Parties agree as follows:

9.2.1. [***].

9.2.2. [***].

9.2.3. [***].

9.2.4. **Reimbursement of Payments**. In the event of an Adverse Alnylam Litigation Impact, if DICERNA fails to [***] DICERNA shall, upon BOEHRINGER's request, reimburse BOEHRINGER the Milestone Payments made by BOEHRINGER to DICERNA in accordance with Article 4.4 of this Agreement (the "**Reimbursement Payments**"). Such Reimbursement Payments shall be made [***] after receipt of a Reimbursement Payment request issued by BOEHRINGER to DICERNA in writing.

9.2.5. [***].

9.3. **Indemnification by BOEHRINGER**. BOEHRINGER shall indemnify, defend, and hold harmless DICERNA and its Affiliates, and its respective officers, governors, employees, licensors, and their respective successors, heirs and assigns and representatives (the "**DICERNA Indemnitees**"), from and against any and all Damages resulting from Third Party Claims against a DICERNA Indemnitee (including by BOEHRINGER employees), to the extent directly or indirectly arising out of or relating to (i) the negligence, recklessness or wrongful intentional acts or omissions of BOEHRINGER, its Affiliates, and its respective licensees, officers, directors, employees in connection with BOEHRINGER's performance of its obligations or exercise of its rights under this Agreement, (ii) any breach by BOEHRINGER of any obligation, representation, warranty or covenant set forth in this Agreement, (iii) the failure to comply with any Applicable Laws by BOEHRINGER, its Affiliates, or any of its licensees or subcontractors, (iv) personal injuries related to or arising out of the development or manufacture of a Product by or on behalf of BOEHRINGER or its Affiliates or licensees, (v) any product liability claim related to or arising out of the use of a Product commercialized by or on behalf of BOEHRINGER or its Affiliates, except in any such case for Damages to the extent such Damage is caused by a DICERNA Indemnitee's negligence or willful misconduct.

9.4. **Notification; Assumption of Defense; Cooperation and Assistance**. In the event that a Party seeks indemnification hereunder with respect to a Third Party claim, proceeding or action (a "**Third Party Claim**"), the Party seeking indemnification (the "**Indemnified Party**") shall promptly notify the other Party (the "**Indemnifying Party**") in writing of any Third Party Claim in respect of which it intends to claim indemnification under this Article 9.4, provided that any failure to provide the Indemnifying Party with any such notice will not relieve the Indemnifying Party from any liability that it may have to the Indemnified Party under this Article 9.4 except to the extent that the ability of the Indemnifying Party to defend such claim is materially prejudiced by the Indemnified Party's failure to give such notice. The Indemnifying Party shall have the right to assume exclusive control of the defense and settlement of the Third Party Claim with counsel reasonably acceptable to the Indemnified Party [***], subject to the limitations on settlement set forth below. If the Indemnifying Party assumes such defense, the Indemnified Party will have the right to participate in the defense thereof and to employ counsel, at its own expense, separate from the counsel employed by the Indemnifying Party. If the Indemnifying Party does not commence actions to assume control of the defense of a Third Party Claim within [***] after the receipt by the Indemnifying Party of the notice required pursuant to this Article 9.4, the Indemnified Party will have the right to defend such claim in such manner as it may deem appropriate at the reasonable cost and expense of the Indemnifying Party. The Indemnified Party shall cooperate as may be reasonably requested in order to ensure the proper and adequate defense of any action, claim or liability covered by this indemnification. The Indemnifying Party may not settle or otherwise dispose of any Third Party Claim without the prior written consent of the Indemnified Party unless such settlement includes only the payment of monetary damages (which are fully paid by the Indemnifying Party), does not impose any injunctive or equitable relief upon the Indemnified Party, does not require any admission or acknowledgment of liability or fault

of the Indemnified Party and contains an unconditional release of the Indemnified Party in respect of such Third Party Claim. The Indemnified Party may not settle or otherwise dispose of any Third Party Claim for which the Indemnifying Party may be liable for damages under this Agreement without the prior written consent of the Indemnifying Party.

10. TERM AND TERMINATION

10.1 **Term**. This Agreement shall commence upon the Effective Date and, if not otherwise terminated earlier pursuant to this Article 10, shall continue in full force and effect until the expiration of the last payment obligation by BOEHRINGER or, if earlier, the date the Evaluation Period expires for the last Candidate Product for all Targets evaluated by BOEHRINGER with BOEHRINGER having selected no Candidate Product to become a Product for a Target (the "**Term**").

10.2 **Termination for Cause.** This Agreement may be terminated in whole or part at any time during the Term of this Agreement by a Party (the "**Non-Defaulting Party**"):

10.2.1 Upon Default by the other Party (the "**Defaulting Party**") which Default remains uncured for [***] measured from the date written notice of such Default is provided to the Defaulting Party. The Non-Defaulting Party shall provide written notice to the Defaulting Party, which notice shall identify the Default, the intent to so terminate and the actions or conduct that it considers would be an acceptable cure of such Default. In case the Defaulting Party disputes the Default under this Article 10.2.1, then the issue of whether the Non-Defaulting Party may properly terminate this Agreement on expiration of the applicable cure period shall be resolved in accordance with Section 11.8. If as a result of such arbitration process, it is determined that the alleged Defaulting Party committed a Default and the Defaulting Party does not cure such Default within [***] after the date of such award, (the "**Additional Cure Period**"), then such termination shall be effective as of the expiration of the Additional Cure Period. If the Parties dispute whether such Default was so cured, either Party alone may request the same arbitrators to determine whether it was so cured, and the Parties shall cooperate to allow such determination to be made within [***] after such request by either Party. Such arbitration proceeding does not suspend any obligations of either Party hereunder, and each Party shall use reasonable efforts to mitigate any damage. If as a result of such arbitration proceeding it is determined that the alleged Defaulting Party did not commit such Default (or such Default was cured in accordance with this Section 10.2.1), then no termination shall be effective, and this Agreement shall continue in full force and effect. Notwithstanding the foregoing, DICERNA shall not have the right to terminate this Agreement for BOEHRINGER's Default following [***], provided that BOEHRINGER pays DICERNA the amount of such damages that have been awarded by an arbitration proceeding pursuant to Section 11.8.

10.2.2 To the extent permitted by Applicable Laws upon the filing or institution of bankruptcy, reorganization, liquidation or receivership proceedings, or upon an assignment of a substantial portion of the assets for the benefit of creditors by the other Party provided, however, that in the case of any involuntary bankruptcy proceeding such right to terminate shall only become effective if the Party consents to the involuntary bankruptcy or such proceeding is not dismissed within [***] after the filing thereof.

10.3 **Termination by BOEHRINGER for Change of Control**. In the event of a Change of Control of DICERNA, BI shall have the right to terminate this Agreement [***] upon [***] prior written notice to DICERNA.

10.4 [***]

10.5 **Termination at Will**. BOEHRINGER shall be entitled to terminate this Agreement forthwith at its sole discretion at any time upon [***] prior written notice to DICERNA thereof.

10.6 **Termination by BOEHRINGER for IP Challenges**. In the event that DICERNA directly or indirectly challenges the Product IP, and/or the BOEHRINGER Product IP including but not limited to patents Covering the composition of matter of a Product, before a patent office, court or other governmental agency of competent jurisdiction (the "**DICERNA IP Challenge**"), BOEHRINGER shall be entitled to terminate this Agreement [***].

10.7 **Effects of Termination by DICERNA for Cause/by BOEHRINGER at Will**. Upon termination of the Agreement by (i) DICERNA pursuant to Section 10.2 or (ii) BOEHRINGER pursuant to Section 10.5:

(a) Each Party shall immediately terminate any activities for any terminated Product, Candidate Product or Target under this Agreement; and

(b) The Receiving Party shall promptly return to the other Party or destroy all Confidential Information of the Disclosing Party in accordance with Section 6.2 above; and

(c) All licenses granted by a Party to the other Party under this Agreement shall immediately terminate; and

(d) DICERNA shall be relieved of the exclusivity under Section 5.10 of this Agreement; and

(e) BOEHRINGER shall be relieved from any and all payment obligations under this Agreement except with respect to obligations resulting from activities that occurred prior to termination; and

(f) Terminated Candidate Products, Products or Targets shall no longer be deemed to be Candidate Products, Products or Targets, respectively, under this Agreement; and

(g) [***].

(h) BOEHRINGER shall assign to DICERNA, free of any liens, DICERNA's original rights, title and interest to the Product IP ([***] provided that BOEHRINGER shall retain a [***] license, [***] to use the Product IP [***].

(i) BOEHRINGER and DICERNA may negotiate in good faith an agreement on (i) a license to use the BOEHRINGER Product IP and/or to BOEHRINGER's remaining rights to Product IP developed jointly by BOEHRINGER and DICERNA solely to develop, manufacture, use, sell, offer for sale, import and commercialize Products included within the scope of such termination, and (ii) the assignment of regulatory filings regarding a Product, such agreement to bear commercially reasonable consideration.

10.8 **Effects of Termination by BOEHRINGER for Cause/for IP Challenges**. If this Agreement is terminated by BOEHRINGER pursuant to Section 10.2 or 10.6 above, in addition to any other remedies available to BOEHRINGER at law or in equity, BOEHRINGER may in its discretion (i) terminate the Agreement in which case the effects described in Section 10.7(a) through and including Section 10.7(g) shall apply, or (ii) exercise an alternative remedy as set forth below in this Section 10.8. For the avoidance of doubt, except as set forth in this Section 10.8, in the event BOEHRINGER exercises the alternative remedy set forth below in this Section 10.8, all rights and obligations of BOEHRINGER under this Agreement shall continue unaffected upon Default by DICERNA or in the event of a Dicerna IP Challenge, respectively, unless this Agreement is subsequently terminated by either Party pursuant to another termination right under this Article 10, as applicable, after BOEHRINGER exercises its rights pursuant to the following sentence: following the occurrence of an event that would allow BOEHRINGER to terminate this Agreement under Section 10.2 or 10.6 and subject to the conditions set forth in such Section 10.2 or 10.6 and if BOEHRINGER elects, the following shall apply as an alternative remedy to such termination right and without consideration (except as otherwise stated below) in lieu of termination of this Agreement:

(i) BOEHRINGER may retain all of its licenses and other rights granted under this Agreement, subject to all of its payment and other obligations; except that the applicable Milestone Payments and the applicable royalty rate payable thereafter under this Agreement shall be reduced by [***]; and

(ii) Any BOEHRINGER Confidential Information provided to DICERNA pursuant to this Agreement will be promptly returned to BOEHRINGER or destroyed; BOEHRINGER shall be released of its ongoing disclosure and information exchange obligations with respect to activities following the effective date of such termination.

10.9 [***]

10.10 **Effects of Termination for Change of Control**. In the event of a termination by BOEHRINGER pursuant to Section 10.3 (i), (ii) or (iii), the provisions of Section 10.7 shall apply accordingly with regard to the scope of such termination.

10.11 **Rights Accruing Prior to Expiration or Termination**. Expiration or termination of this Agreement shall not relieve the Parties of any obligation accruing prior to such expiration or termination. Any expiration or termination of this Agreement shall be without prejudice to the rights of either Party against the other accrued or accruing under this Agreement prior to expiration or termination, including the obligation to pay for any amounts that accrued prior to the effective date of such expiration or termination.

10.12 **Survival**. In addition to any provisions specified in this Agreement as surviving as set forth therein, the provisions of Articles 1, 6 (for the period stipulated in Section 6.11 above), 8, 9 and 11 and Sections 4.7, 4.8, 4.12 through and including 4.21, 7.4.4 (each in the event of payment obligations resulting from activities that occurred prior to termination), Sections 5.9, 5.12, 5.13, 5.14.7, 7.1, 7.2.5 and 7.3.4 shall survive any termination or expiration of the Agreement. In addition, all rights and obligations contained in this Agreement, which by their nature or effect contemplate performance or observance subsequent to expiration or termination of this Agreement will survive and remain binding upon and for the benefit of the Parties, their successors and permitted assigns.

11. CONCLUDING PROVISIONS

11.1 **Assignment**. Neither Party shall be entitled to assign or otherwise transfer its rights and/or obligations under this Agreement in whole or in part to any Third Party without the prior written consent of the other Party, which consent shall not be unreasonably withheld, provided that, however, each Party may assign this Agreement to (i) any Affiliate, and (ii) any successor corporation or entity resulting from any Change of Control of such Party, and provided that the Affiliate, entity or Third Party to which this Agreement is assigned expressly agrees in writing to assume and be bound by all obligations of the assigning Party under this Agreement. The Parties agree that in no event shall BOEHRINGER assign its rights and/or obligations under this Agreement [***]. Each Party agrees to be responsible for the actions and omissions of its Affiliates under this Agreement.

11.2 **Entire Agreement; Amendments**. This Agreement sets forth the entire agreement between the Parties and supersedes all previous and contemporaneous negotiations, representations or agreements, written or oral, regarding the subject matter hereof. This Agreement may be amended only by an instrument in writing duly executed on behalf of the Parties. In case of inconsistencies between this Agreement and any Appendix hereof, the terms of this Agreement shall prevail unless agreed to explicitly that the Appendix should prevail.

11.3 **Force Majeure**. Neither Party shall be liable or deemed in default for failure to perform any duty or obligation that such Party may have under this Agreement where such failure has been occasioned by any act of God, fire, external strike, inevitable accidents, war, or any other cause outside the reasonable control of that Party, and occurring without its fault or negligence. The Party whose performance has so been interrupted shall give the other Party notice of the interruption and cause thereof, and shall use every reasonable means to resume full performance of this Agreement as soon as possible.

11.4 **Waiver**. The failure of either Party to require performance by the other Party of any of that other Party's obligations under this Agreement shall in no manner affect the right of such Party to enforce the same at a later time. No waiver by any Party of any condition, or of the breach of any provision, term, representation or warranty contained in this Agreement shall be deemed to be or construed as a further or continuing waiver of any such condition or breach, or of any other condition or of the breach of any other provision, term, representation, or warranty hereof. The remedies provided in this Agreement are not exclusive and the Party suffering from a breach or default of this Agreement may pursue all other remedies, both legal and equitable, alternatively or cumulatively.

11.5 **Severability**. In the event that any provision or portion thereof in this Agreement is for any reason held to be invalid, illegal or unenforceable, the same shall not affect any other portion of this Agreement and its validity, as it is the intent of the Parties that this Agreement shall be construed in such fashion as to maintain its existence, validity and enforceability to the greatest extent possible. In any such event, this Agreement shall be construed as if such provision of portion thereof had never been contained in this

Agreement, and there shall be deemed substituted therefore such provision as will most nearly carry out the intent of the Parties as expressed in this Agreement to the fullest extent permitted by Applicable Law unless doing so would have the effect of materially altering the right and obligations of the Parties in which event this Agreement shall terminate and all the rights and obligations granted to the Parties hereunder shall cease and be of no further force and effect.

11.6 **Notices**. Any notices and Invoices given under this Agreement [***] shall be addressed as follows (or at such other address for a Party as shall be specified by like notice, provided, however, that notices of a change of address shall be effective only upon receipt thereof):

If to DICERNA:

Dicerna Pharmaceuticals, Inc.
87 Cambridgepark Drive
Cambridge, MA 02140
Attention:President and Chief Executive Officer
Facsimile:(617) 612-6298
E-mail:dfambrough@dicerna.com

With a copy to:

Dicerna Pharmaceuticals, Inc.
87 Cambridgepark Drive
Cambridge, MA 02140
Attention: Legal Department

If to BOEHRINGER:

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11.7 **Governing Law**. This Agreement shall be construed in accordance with and governed exclusively by the law of [***], without reference to its rules of conflict of law.

11.8 **Dispute Resolution; Arbitration.** Any dispute arising out of or in connection with this Agreement shall be settled, if possible, through good faith negotiations between the Parties. If the Parties are unable to settle such dispute within [***], such dispute arising out of or relating to this Agreement shall be referred to the Chief Executive Officer of DICERNA or the authorized designee of the Chief Executive Officer of BOEHRINGER (the "**Executive Officers**"). The Executive Officers of both Parties shall meet to attempt to resolve such dispute. Such resolution, if any, of a referred issue shall be final and binding on the Parties. All negotiations pursuant to this Section 11.8 are confidential and shall be treated as compromise and settlement negotiations for purposes of applicable rules of evidence. If the Executive Officers cannot resolve such dispute within [***] after either Party requests such a meeting in writing, then the Parties agree that all disputes that may not be resolved amicably between the Parties arising out of or in connection with this Agreement shall be finally settled under the Rules of Arbitration of the International Chamber of Commerce ("**ICC**") by [***] appointed in accordance with said rules. The exclusive place of arbitration shall be [***] and the proceedings shall be conducted in English language. The award for arbitration shall be final and binding and may be enforced in any court of competent jurisdiction against BOEHRINGER or DICERNA. Notwithstanding the foregoing but without abrogating the agreement of the Parties to binding arbitration, the Parties shall each be entitled either prior to or during arbitration to seek and obtain injunctive or other equitable relief in any court of competent jurisdiction to preserve the status quo (including to enforce the and prevent unauthorized disclosures of Confidential Information or infringement or misappropriation of any Intellectual Property) pending arbitration or to prevent the breach of this Agreement, without the necessity of posting any bond.

The Parties further agree that

(a) except as may be otherwise required by law, neither Party, its witnesses, or the arbitrators may disclose the existence, content, results of the arbitration hereunder without prior written consent of both Parties; and

(b) neither Party shall be required to give general discovery of documents, but may be required only to produce specific, identified documents which are relevant or considered relevant by the arbitrators to the dispute (subject to Third Party confidentiality obligations); and

(c) the scope of authority of the arbitrators should be limited to the strict application of law; and

(d) no arbitrator shall be an employee, director or shareholder of either Party or any of their affiliated companies but each shall have experience in the pharmaceutical industry; and

(e) the chairman shall be a lawyer and not be a national of the country of one of the Parties; and

(f) this Section 11.8 shall apply to any claims by or against the parents, subsidiaries, affiliates, agents, principals, officers, directors, or employees of the Parties; and

(g) the arbitrators may render early or summary disposition of some or all issues, after the parties have had a reasonable opportunity to make submissions on these issues.

11.9 **Independent Contractors**. In the performance of this Agreement each Party shall be an independent contractor and that the relationship between the Parties shall not constitute a partnership, joint venture or agency. Therefore, no Party shall be entitled to any benefits applicable to any employees of the other Party. No Party is authorized to act as an agent for the other Party for any purpose, and no Party shall enter into any contract, warranty, representation, or commitment of any kind as to any matter on behalf of the other Party, without the prior written consent of the other Party.

11.10 **Third Party Beneficiaries**. None of the provisions of this Agreement shall be for the benefit of or enforceable by any Third Party, including, without limitation, any creditor of either Party. No such Third Party shall obtain any right under any provision of this Agreement or shall by reasons of any such provision make any claim in respect of any debt, liability or obligation (or otherwise) against either Party.

11.11 **Non-Employment**. Each Party shall at all times be and remain the sole employer of persons assigned to the performance of work by such Party hereunder and shall assume any and all obligations, responsibilities and risks to such employment and the possible termination thereof.

11.12 **Headings.** The captions to the Articles and Sections of this Agreement are not a part of this Agreement, but are merely for convenience to assist in locating and reading the several Sections of this Agreement.

11.13 **Further Assurances**. Each of DICERNA and BOEHRINGER agrees to duly execute and deliver, or cause to be duly executed and delivered, such further instruments and do and cause to be done such further acts and things, including, without limitation, the filing of such additional assignments, agreements, documents and instruments, as the other Party may at any time and from time to time reasonably request in connection with this Agreement or to carry out more effectively the provisions and purposes of, or to better assure and confirm unto such other Party its rights and remedies under, this Agreement. Each person executing this Agreement on behalf of a Party represents and warrants his/her capacity and authority to do so.

IN WITNESS WHEREOF, the Parties have executed this Agreement in duplicate originals by their duly authorized representatives as of the date and year first above written

Boehringer Ingelheim International GmbH

By: /s/ Jürgen Beck

Name: Jürgen Beck

Title: Authorized Signatory

Boehringer Ingelheim International GmbH

By: /s/ Dorothee Schwall-Rudolph

Name: Dorothee Schwall-Rudolph

Title: Authorized Signatory

Dicerna Pharmaceuticals Inc.

By: /s/ John B. Green

Name: John B. Green

Title: Chief Financial Officer

Appendices:
Appendix 1: Research Work Plan
Appendix 2: Development Plan
Appendix 3: Contact List
Appendix 4: Requirements for Invoices

APPENDIX 1

Research Work Plan

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*****Text Omitted and Filed Separately with the Securities and Exchange Commission. Confidential Treatment Requested Under 17 C.F.R. Sections 200.80(b)(4) and 240.24b-2**

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APPENDIX 2

Development Plan

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*****Text Omitted and Filed Separately with the Securities and Exchange Commission. Confidential Treatment Requested Under 17 C.F.R. Sections 200.80(b)(4) and 240.24b-2**

APPENDIX 3

Contact List

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APPENDIX 4
Requirements for Invoices

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Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement Nos. 333-202687 and 333-214082 on Form S-3 and in Registration Statement Nos. 333-193795 and 333-210071 on Form S-8 of our report dated March 8, 2018, relating to the consolidated financial statements of Dicerna Pharmaceuticals, Inc. and its subsidiaries appearing in this Annual Report on Form 10-K of Dicerna Pharmaceuticals, Inc. for the year ended December 31, 2017.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 8, 2018

Exhibit 31.1

CERTIFICATIONS

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

1. I have reviewed this Annual Report on Form 10-K of Dicerna Pharmaceuticals, Inc. for the year ended December 31, 2017;

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

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

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

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

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

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

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

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

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

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

Date: March 8, 2018

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

Exhibit 31.2

CERTIFICATIONS

I, John B. Green, certify that:

1. I have reviewed this Annual Report on Form 10-K of Dicerna Pharmaceuticals, Inc. for the year ended December 31, 2017;

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

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

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

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

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

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

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

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

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

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

Date: March 8, 2018

/s/ John B. Green
John B. Green
Chief Financial Officer

Exhibit 32.1

SECTION 1350 CERTIFICATIONS*

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

1. The Company's Annual Report on Form 10-K, for the year ended December 31, 2017, to which this Certification is attached as Exhibit 32.1 (the "Annual Report"), fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

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

Dated: March 8, 2018

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

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