Dicerna Pharmaceuticals Inc
Form 10-K
March 27, 2014
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

Form 10-K

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

For the fiscal year ended December 31, 2013

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.)**

480 Arsenal Street,

Building 1, Suite 120

Watertown, MA 02472

(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 x

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 x

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 x

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, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ¨	Accelerated filer ¨
Non-accelerated filer x (Do not check if a smaller reporting company)	Smaller reporting company ¨

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

The registrant completed the initial public offering of its common stock, par value $0.0001 per share, on February 4, 2014. There was no public market for the registrant s common stock as of June 28, 2013, the last business day of the registrant s most recently completed second fiscal quarter. As of March 26, 2014, there were 17,755,204 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of registrant s definitive proxy statement to be filed for its 2014 Annual Meeting of Stockholders are incorporated by reference into Part III hereof. Such proxy statement will be filed with the Securities and Exchange Commission within 120 days of the end of the fiscal year covered by this Annual Report on Form 10-K.

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DICERNA PHARMACEUTICALS, INC.

2013 ANNUAL REPORT ON FORM 10-K

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

- the initiation, timing, progress and results of our research and development programs, preclinical studies, any clinical trials and Investigational New Drug application, New Drug Application and other regulatory submissions;
- our dependence on our existing collaborator, Kyowa Hakko Kirin Co., Ltd. (KHK), for developing, obtaining regulatory approval for and commercializing product candidates in the collaboration;
- our receipt and timing of any milestone payments or royalties under our research collaboration and license agreement with KHK or arrangement with any future collaborator;
- our ability to identify and develop product candidates for treatment of additional disease indications;
- our or a collaborator s ability to obtain and maintain regulatory approval of any of our product candidates;
- the rate and degree of market acceptance of any approved products candidates;
- the commercialization of any approved product candidates;
- our ability to establish and maintain additional collaborations and retain commercial rights for our product candidates in the collaborations;
- the implementation of our business model and strategic plans for our business, technologies and product candidates;
- our estimates of our expenses, ongoing losses, future revenue and capital requirements;

our ability to obtain additional funds for our operations;

our ability to obtain and maintain intellectual property protection for our technologies and product candidates and our ability to operate our business without infringing the intellectual property rights of others;

our reliance on third parties to conduct our preclinical studies or any future clinical trials;

our reliance on third party supply and manufacturing partners to supply the materials and components for, and manufacture, our research and development, preclinical and clinical trial drug supplies;

our ability to attract and retain qualified key management and technical personnel;

our expectations regarding the time during which we will be an emerging growth company under the Jumpstart Our Business Startups Act;

our financial performance; and

developments relating to our competitors or our industry.

These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations

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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 and the Company re to Dicerna Pharmaceuticals, Inc. and, where appropriate, its consolidated subsidiary.

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.

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PART I

Item 1. ***Business***

We are a biopharmaceutical company focused on the discovery and development of innovative treatments for rare inherited diseases involving the liver and for cancers that are genetically defined. We are using our proprietary RNA interference (RNAi) technology platform, which we believe improves on existing RNAi technologies, to build a broad pipeline in these therapeutic areas. In both rare diseases and oncology, we are pursuing targets that have historically been difficult to inhibit using conventional approaches, but where we believe connections between targets and diseases are well understood and documented. We aim to discover, develop and commercialize novel therapeutics either on our own or in collaboration with pharmaceutical partners. In indications such as rare diseases in which a small sales force will suffice, we seek to retain substantially all commercial rights in key markets. In oncology and other more prevalent disease areas, we may partner our product candidates while seeking to retain significant portions of the commercial rights in North America. We have partnered two of our oncology development programs with the global pharmaceutical company Kyowa Hakko Kirin Co., Ltd. (KHK). We are eligible to receive royalties on worldwide net sales for these product candidates. We have an option to co-promote any product candidate targeting the oncogene KRAS, the more advanced of these two programs, in the U.S. for an equal share of the profits from U.S. net sales.

In choosing which programs to advance, we apply scientific, clinical and commercial criteria that we believe will allow us to best leverage our RNAi platform and maximize value for our company. Our current development programs are as follows.

DCR-PH1 for Primary Hyperoxaluria 1 (PH1). We are developing DCR-PH1 for the treatment of the rare and serious inherited disorder PH1 by targeting the liver metabolic enzyme glycolate oxidase. In the mouse genetic model of PH1, we have shown that by using our RNAi technology to inactivate the gene encoding glycolate oxidase we can significantly reduce the key pathology of PH1. We seek to begin clinical trials for DCR-PH1 in 2015.

Other rare inherited diseases involving the liver. We are investigating a number of other rare diseases involving disease target genes expressed in the liver, using a variety of criteria to assess the clinical need, applicability of our RNAi platform, feasibility of development, and market potential. Based on the investigation results, we plan to select one or more specific diseases or disorders for which we will seek to research and develop drug candidates based on our platform.

DCR-M1711 for MYC-related cancers. We are developing DCR-M1711 for the treatment of various cancers by targeting the MYC oncogene, a gene that causes or promotes cancer when abnormally expressed or activated. The expression of MYC is increased in a wide variety of tumor types. Abundant genetic data implicates the MYC oncogene in promoting tumors and inhibition of MYC has exhibited strong anti-tumor effects in numerous animal models of human cancers. We expect to initiate clinical trials for DCR-M1711 in the first half of 2014. We intend to investigate DCR-M1711 in a variety of tumor types. Our initial focus is on hepatocellular carcinoma (HCC) We submitted an Investigational New Drug (IND) application for DCR-M1711 for the treatment of solid tumors to the U.S. Food and Drug Administration (FDA) in the first

quarter of 2014 and have received from the FDA a non-objection letter to initiate the Phase 1 development.

Two product candidates in collaboration with KHK, including one for KRAS-related cancers. We are developing a product candidate targeting the oncogene KRAS in collaboration with KHK. KRAS is frequently mutated in numerous major cancers, including non-small cell lung cancer, colorectal cancer and pancreatic cancer. Such KRAS mutations are associated both with more aggressive disease as well as with resistance to current therapies. We are also developing a second product candidate targeting an oncogene in collaboration with KHK. With respect to both product candidates in collaboration, KHK is responsible for selecting clinical product candidates, all preclinical and clinical development activities and the choice of patient population and disease indications for clinical trials pursuant to the terms of our collaboration.

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All of our 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 biological process certain double-stranded RNA molecules induce the potent and specific enzymatic destruction of the messenger RNAs (mRNAs) of target genes containing sequences that are complementary to one strand of the therapeutic double-stranded RNA molecule. Our discovery approach is based on double-stranded RNAs that we believe maximize RNAi potency as they represent what we believe are optimal molecules for the RNAi initiating enzyme Dicer. We refer to these proprietary RNAi molecules as Dicer substrates, or DsiRNAs.

RNAi reflects a new approach in the development of specific and powerful targeted therapies against both rare diseases and cancer. Historically, the pharmaceutical industry has brought forward two classes of drugs to seek to address well-defined targets: small molecules and antibodies. Each of these drug classes has been very successful. However, both are limited in the nature of the targets they can inhibit. Small molecules need to make their way to specific binding pockets of protein targets, and many disease-associated proteins lack small molecule binding pockets. Antibody therapeutics, while highly successful, are limited to easily accessible targets found in circulation or expressed outside of cells.

RNAi offers the potential to go beyond both of these therapeutic modalities and attack targets such as transcription factors, proteins lacking good small-molecule binding pockets and expressed exclusively inside cells that control which genes are turned on or off in the genome. Some of these targets have been known for decades and are considered to be highly attractive targets for drug development. Targets such as MYC and KRAS have been shown to be oncogenes that are critical drivers of cancer formation in both animal models and humans. However, due to the limitations of conventional therapeutics, the pharmaceutical industry has been unable to develop molecules that target them. They have become widely identified as undruggable.

We believe that DsiRNAs provide the following qualities and advantages for triggering RNAi compared to other types of double-stranded RNAs used to induce RNAi.

We initiate RNAi through the Dicer enzyme. DsiRNAs are structured to be ideal for processing 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 a Dicer enzyme processing event, DsiRNAs enter the RNAi pathway at this natural initiation point. This property allows us to drive preferential use of the correct RNA strand of the DsiRNA, which may increase the efficacy of the RNAi mechanism. This benefit may increase the potency of our DsiRNA molecules relative to other molecules used to induce RNAi, and so potentially enable many more sequences to be used to generate potent DsiRNAs compared to other RNAi-inducing molecules.

We use a proprietary delivery system. We have developed EnCore lipid nanoparticles, a proprietary and effective system for the delivery of our DsiRNAs to liver tissues and to solid tumors. We believe our EnCore lipid nanoparticles can effectively deliver our DsiRNAs, have low toxicity and are amenable to manufacturing in large scale. We have been able to, even at doses as low as 13.1μg/kg, induce silencing of gene expression at the 50 percent level, which we believe is below the dose level at which we would expect to see dose-limiting toxicity. Other RNAi molecules in development are delivered by a variety of methods, including other types of lipid nanoparticles, nanoparticle systems that use polymers instead of lipids, and non-nanoparticle methods involving conjugation of the RNAi molecules to molecular targeting agents.

Our molecules have two conjugation points, which are cleaved off by the Dicer enzyme, allowing for direct delivery. Due to the way that the Dicer enzyme processes our DsiRNAs, we believe our molecules could potentially provide advantages for targeted delivery methods that do not use lipid nanoparticles. Our DsiRNAs have two distinct conjugation points at the blunt end of the double-stranded RNA. At this blunt end the two strands of the DsiRNA can be conjugated to a targeting agent and an endosomal escape agent, respectively. We believe these agents allow the DsiRNA to be targeted to specific cell types and to enter the cytoplasm of the cell, with the targeting agent mediating cell

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binding and internalization, and the endosomal escape agent mediating cytoplasmic release. After delivery to the cytoplasm, the Dicer enzyme cleaves the molecule just as with an unconjugated DsiRNA. Because of this quality, our targeted delivery methods are able to use covalent chemical linkers that we believe are more easily synthesized directly into the RNA strand, facilitating delivery and enhancing the drug-like properties of the molecules. We have shown in cell free systems that both conjugation points on our DsiRNAs can be used simultaneously without inhibiting processing by the Dicer enzyme. We anticipate that our future product candidates may utilize these conjugation points to improve further the delivery of our DsiRNAs. We are currently working to develop delivery technologies using this approach to directly deliver our DsiRNAs subcutaneously to liver tissues and ultimately to solid tumors.

We believe that we have a robust patent portfolio directed to our proprietary position for our RNAi technology platform and product candidates. We own three U.S. patents and a significant number of pending patent applications that cover various aspects of our RNAi technology and our discovery platform, including our proprietary DsiRNA molecules. We also own numerous patent applications covering specific DsiRNA sequences that drive activity against high value disease targets, including MYC, KRAS and others. Furthermore, we own seven U.S. patents and numerous patent applications related to our EnCore delivery technology.

Our executive management team has more than 76 years of collective 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 Alnylam Pharmaceuticals, Inc., Genta Incorporated, GlaxoSmithKline plc, Pfizer Inc., Sirna Therapeutics, Inc. (which was acquired by Merck & Co., Inc. in 2006 and recently sold by Merck & Co., Inc. to Alnylam Pharmaceuticals, Inc. in March 2014) 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 Therapeutics, an early RNAi company that was acquired by Merck & Co., Inc. in 2006 for $1.1 billion. He played a pivotal role not only in managing the investment but also in restructuring Ribozyme Pharmaceuticals, Sirna Therapeutics predecessor company, as well as executing the acquisition by Merck & Co., Inc. in 2006.

Strategy

We are committed to delivering transformative therapies to patients with life-threatening conditions. The key elements of our strategy are as follows.

Validate our product candidates and our platform in clinical proof-of-concept studies. Beginning in the first half of 2014, we plan to conduct clinical trials that we believe may generate human proof-of-concept data. We seek to maximize the likelihood of success in those trials by: (1) using genetic analysis, if necessary, to identify a target population that is likely to respond to our therapeutics and (2) observing biomarkers and other markers as indications of efficacy at an early stage. Based on precedents in the RNAi field, we anticipate that data showing the destruction or knockdown of target mRNA molecules induced by double-stranded RNA molecules at preclinical dose levels may translate into clinical results. We seek to initiate clinical trials for DCR-M1711 in the first half of 2014 and for DCR-PH1 in 2015.

Identify new indication areas with high unmet medical need. We intend to continue to use our DsiRNA molecules and our drug delivery technology platform to create new, high value pharmaceutical development programs. Our primary focus will remain: (1) rare inherited diseases involving the liver and (2) genetically-defined oncogene targets in oncology. We have discovery and early development projects

against a series of additional disease targets in the liver that meet our target selection criteria. We also continue to explore well known and frequently mutated oncogenes that are critical drivers of cancer formation such as CTNNB1 (also known as ß-catenin).

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Continue to develop product candidates for rare diseases and oncology while retaining meaningful commercial rights. We seek to maintain significant commercial rights to our key development programs. In the rare disease area, such as PH1, we seek to retain full commercial rights in the United States and potentially in other key markets. In oncology, we may partner our product candidates while retaining certain commercial rights in North America. For example, in our collaboration with KHK, we have an option to co-promote the product candidate targeting KRAS in the U.S. for an equal share of profits from U.S. net sales.

Enter into additional partnerships with pharmaceutical companies either on our RNAi technology platform or specific indications outside of our core therapeutic areas. We may choose to establish platform or specific target partnerships with pharmaceutical companies across multiple indication areas depending on the attractiveness of the opportunities. These partnerships may provide us with funding to advance our proprietary product candidates and access to development, manufacturing and commercial expertise and capabilities.

Continue to invest in our RNAi technology platform. We plan to continue to invest in expanding and improving our DsiRNA molecules and our EnCore and other delivery technologies in order to develop new product candidates in indications that we are currently exploring and that we intend to explore in the future. Building on what we believe are our advantages in potency and delivery, we seek to develop product candidates that will have a dramatic impact on the RNAi field.

Our RNAi Technology Platform

All of our 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. The RNAi process is triggered by double-stranded RNA molecules containing sequences that are complementary to the sequence of the targeted gene. Our novel and highly potent approach is based on double-stranded RNAs that are aimed to serve as optimal molecules for the RNAi initiating enzyme Dicer, and thus our proprietary RNAi molecules are known as Dicer substrates, or DsiRNAs. The RNAi machinery, guided by a DsiRNA (or other double-stranded RNAi-inducing molecules) causes the targeted destruction of specific mRNA molecules of the complementary target gene. Destroying these mRNA molecules immediately decreases the biological activity from the target gene. A single DsiRNA incorporated into the RNAi machinery can destroy hundreds or thousands of mRNAs from the targeted gene.

We believe that our DsiRNAs have distinct traits in triggering the RNAi pathway to silence certain disease-driving genes, which may provide advantages for triggering RNA interference compared to other types of double-stranded RNAs used to induce RNAi. Our DsiRNAs are structured to be optimal for processing by the Dicer enzyme. We believe that other RNAi-inducing molecules currently in development mimic the output of a Dicer enzyme processing event, and thus act at a later point in the RNAi pathway. By contrast, DsiRNAs enter the RNAi pathway through being presented to Dicer itself, the pathway s natural initiation point. By entering the RNAi pathway at that point, we believe that DsiRNAs are able to maximize the efficacy of the RNAi mechanism, making DsiRNAs potentially more potent than traditional RNAi-inducing molecules. This potential potency advantage derives from the structure of the DsiRNA molecule and how it interacts with the Dicer enzyme. Specifically, the structure of the DsiRNA is able to indicate to the Dicer enzyme which of the two RNA strands should be used to guide the selective destruction of disease gene target mRNAs by the RNAi machinery. We have found in animal tests that this benefit both increases the potency of our DsiRNA molecules relative to other RNAi-inducing molecules and enables many more sequences to be used to generate our potent DsiRNAs compared to other RNAi-inducing molecules. We therefore believe that the nature of the interaction of our DsiRNAs with the RNAi pathway intervention facilitates the discovery of new DsiRNA

therapeutic candidates and further strengthens our intellectual property position.

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Schematic representation of our DsiRNA

DsiRNAs are precisely-sized double-stranded RNA molecules that are asymmetric. In the standard form we use for our therapeutic programs, the longer strand is 27 bases long and is complementary to the target gene we seek to silence, known as the Guide Strand. The shorter strand is 25 bases long and known as the Passenger Strand. The two strands are complementary across their length, with the two additional bases of the 27-mer forming a two-base overhang at the 3 -end of the molecule. For our product candidates using our EnCore lipid nanoparticle delivery technology, we chemically modify some of the RNA bases and we also use two bases of DNA at the 3 end of the Passenger Strand (denoted by black circles). These DNA bases, along with the two-base overhang on the 27-mer, cause the Dicer enzyme to preferentially take up the Guide Strand.

In addition, due to the nature of how the Dicer enzyme processes a DsiRNA, our DsiRNA molecules may provide advantages for targeted delivery methods that do not use lipid nanoparticles. Our DsiRNA molecules present two distinct chemical conjugation points, which can be used to attach targeting agents or other agents that facilitate delivery or enhance the drug-like properties of the molecules. We have shown that both conjugation points can be used simultaneously without inhibiting processing by the Dicer enzyme. Due to how the Dicer enzyme processes a DsiRNA, we can use stable covalent non-cleavable linkers instead of less stable cleavable linkers that other RNAi molecules may require. We anticipate that our future development programs may utilize these conjugation points to improve further the delivery of our DsiRNAs.

Optimization of our DsiRNAs

For therapeutic use in humans, we believe that our DsiRNAs must be optimized both with respect to base sequence and with respect to chemical modifications to increase stability and to mask them from mechanisms that recognize foreign RNAs, inducing immune system stimulation. Using our proprietary algorithms and screening systems, we have routinely identified and tested DsiRNAs that have achieved high potency and high stability in *in vitro* studies. Furthermore, our research and testing to date suggests that our optimized DsiRNAs may be less likely to induce an immune system response in humans.

Our drug delivery technologies

Our process of delivery

From the initial discovery of the RNAi pathway in mammals through more recent attempts at creating RNAi-based therapeutics, drug delivery has been a profound challenge. Double stranded RNAs, such as our DsiRNAs, are unable to enter cells on their own, but cell entry is required to access the RNAi machinery in the cytoplasm and thus to silence the respective target genes. An effective drug delivery technology is required to ferry the DsiRNA into cells, through the cell internalization pathway and ultimately release the DsiRNA into the cell cytoplasm. Creating all the required steps in a predictable way and creating an industrial process that is scalable and economically feasible has posed a challenge in pursuing RNAi-based therapeutics. We believe that our drug delivery technologies may overcome these challenges.

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RNAi drug delivery requires the following three steps for our DsiRNA molecules to be processed and incorporated into the RNAi machinery.

Step 1. Accumulation in the target tissue.

Step 2. Binding to and internalization by the target tissue cells.

Step 3. Release from the internalization compartment into the cytoplasm.

With other pharmaceuticals, simply accumulating a large enough quantity of a drug in the target tissue is sufficient to achieve a biological effect. But with RNAi-based therapeutics, accumulation alone is inadequate for delivery of RNAi. Active processes are required to get RNAi molecules to the cytoplasm. This requires internalization through the cellular internalization pathway and subsequent release from the internalization compartment (the endosome) into the cytoplasm. An effective RNAi delivery mechanism needs to mediate these processes of accumulation, internalization and release into the cytoplasm to achieve successful drug delivery of DsiRNAs.

EnCore lipid nanoparticles are composed of a lipid-DsiRNA core surrounded by an envelope of different lipids which mediate the accumulation, internalization and release into the cytoplasm of the DsiRNA in the core of the particle.

EnCore lipid nanoparticles

We believe that our EnCore lipid nanoparticles effectively mediate all three steps required for delivery of our DsiRNA product candidates: accumulation, internalization and release into the cytoplasm. Our EnCore lipid nanoparticles not only perform these three functions but we believe also could have beneficial properties such as high tolerability (low toxicity), ease of manufacturing, effective DsiRNA loading and protection of the DsiRNA payload. We have successfully demonstrated each of these properties of EnCore lipid nanoparticles and have used them to achieve delivery of our DsiRNAs in animal models. Based on the results of our studies, we also believe that we can adjust the composition of the EnCore lipid nanoparticles to mediate delivery of the DsiRNA payload to the liver or to other tissues, including tumors.

Highly potent delivery of DsiRNA

To demonstrate the efficiency of EnCore in mediating the effective delivery of DsiRNAs in animals, we have used EnCore in the industry standard Factor VII inhibition assay. We have packaged in EnCore a DsiRNA targeting the gene encoding the Factor VII serum protein, which is highly expressed in the liver. These DsiRNA-EnCore lipid nanoparticles were administered intravenously to mice in varying doses, to measure the dose response of Factor VII silencing. We have found that doses as low as 13.1μg/kg of DsiRNA can produce silencing at the 50 percent level (the EC50 dose, used for comparison between delivery systems). This represents highly potent delivery of DsiRNAs to the liver.

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EnCore performance in an industry standard assay

EnCore lipid nanoparticles mediate silencing of the Factor VII gene in mice at low doses. EnCore delivered DsiRNA against the Factor VII gene mediates 50 percent silencing of Factor VII at doses of 13.1 µg/kg. A conventional RNAi-inducing molecule of the same sequence as the DsiRNA, known as a siRNA, is less potent and mediates 50 percent silencing of Factor VII at doses of 32.6 µg/kg.

Subcutaneous Direct Targeted Delivery of DsiRNAs using conjugation

We believe that the structure of DsiRNAs is well suited for direct conjugation to delivery agents, using the blunt end of the double stranded RNA. We are working to develop an additional delivery system based on this direct conjugation in which the end of the DsiRNA is cleaved off by Dicer in the cytoplasm, removing the conjugated agents so that they do not interfere with the RNAi machinery. We call this system of delivering DsiRNA by conjugated agents our Direct Targeted Delivery system. If our development efforts are successful, this system could provide for generalized subcutaneous delivery of DsiRNAs to various cell types throughout the body, as we believe that these molecules could have broad biodistribution, similar to monoclonal antibodies.

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Our Product Candidates

In choosing clinical programs to pursue using our DsiRNA molecules and drug delivery technologies, we apply various criteria including clinical need, applicability of our RNAi platform, feasibility of development, and market potential. The programs we have so far selected by this approach, and their current status, are summarized below:

DCR-PH1 in Primary Hyperoxaluria 1 (PH1)

PH1 is a rare, inherited autosomal recessive disorder of metabolism in the liver that usually results in severe damage to the kidneys. The disease can be fatal in the absence of an intervention in the form of a liver-kidney transplant, itself a risky procedure that presents a challenge in identifying a donor and is associated with high co-morbidity rates. Currently, even when a transplant is successfully performed, the patient must live the rest of his or her life on immunosuppressant drugs with their associated risks.

PH1 is caused by the failure of the liver to metabolize a precursor of oxalate, a highly insoluble metabolic end-product in humans, resulting in excess oxalate and high levels of oxalate in the urine. This oxalate is formed during the metabolic breakdown of hydroxyproline, a naturally occurring component of collagen. In individuals with PH1, crystals of calcium oxalate form in the renal tubules, leading to chronic and painful cases of kidney stones and subsequent fibrosis, known as nephrocalcinosis. Despite the typical interventions of a large daily intake of water to dilute the oxalate and other interventions, many patients eventually enter end-stage renal disease (ESRD) and become eligible for transplant. While in ESRD, besides having to endure frequent dialysis, patients are afflicted with a build-up of oxalate in the bone, skin, heart and retina with concomitant debilitating complications. We believe that currently, aside from dual-organ transplant, there are no highly efficacious therapeutic options for most patients with PH1. Some patients show partial disease amelioration with oral pyridoxine supplementation, although disease progression usually continues. Supportive care treatments are available, generally with only minor or no effect on disease progression. Even in those U.S. patients treated with dual-organ transplant, five-year post-transplant survival is 64 percent. For patients treated with kidney transplant alone, five-year survival is 45 percent.

While the true prevalence of PH1 is unknown, according to estimates recently published by the New England Journal of Medicine, the prevalence of PH1 is at least one to three per million of population. Based on the frequency of occurrence of disease mutations in the population, the expected genetic incidence is eight per million of population, which we believe suggests that PH1 is under-diagnosed. The disease is thought to have an incidence of one per 120,000 live births a year in Europe. Certain populations, for example in the Canary Islands (Spain) or

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Kuwait, have higher incidences due to founder effects or consanguinity. We believe approximately 800 patients are currently registered in one of two distinct disease registries in North America and Europe, although these registries do not capture all afflicted patients. Prevalence is believed to be similar in Asia. Given the severity of PH1, we believe this disease represents a significant market opportunity. The patient advocacy group, the Oxalosis and Hyperoxaluria Foundation, based in New York City, New York, seeks to represent patients with PH1.

Therapeutic rationale for PH1

We believe that there is a strong rationale for focusing our RNAi technology to develop product candidates for the treatment of PH1. The hydroxyproline breakdown metabolic pathway that is disrupted in PH1 consists of a number of enzymes. The ultimate enzyme in the pathway, alanine-glyoxylate aminotransferase 1 (AGT1), is mutated in patients with PH1. Under normal circumstances, AGT1 metabolizes oxalate precursors into the harmless amino acid glycine, which is then used by the body or excreted. But when AGT1 is mutated, oxalate begins to build up, resulting in progressive loss of kidney function and, ultimately, kidney failure. Approximately 50 percent of PH1 patients have kidney failure by age 30 to 35.

Animal studies have shown that intervening one step earlier in the metabolic pathway can reduce or eliminate the abnormally high oxalate production caused by the absence of the AGT1 enzyme. These studies employ mice in which the gene encoding AGT1 has been genetically deleted to create an animal model of PH1. Similar to human patients, these mice have elevated levels of oxalate in their urine. When the enzyme one step earlier in the metabolic pathway than AGT1 is eliminated by genetic deletion in this animal model of PH1, oxalate levels in the urine are substantially reduced. The enzyme upstream of AGT1 is known as glycolate oxidase (GO) and is encoded by the gene HAO1. In normal animals and humans HAO1 is expressed exclusively or nearly exclusively in the liver. We believe that by reducing the amount of HAO1 produced in the liver, a DsiRNA drug targeting this enzyme will reduce the amount of harmful oxalate present in the urine of PH1 patients, mirroring the effect seen in the animal model when the amount of HAO1 was reduced by genetic deletion.

Preclinical data for DCR-PH1

We are using our DsiRNA and EnCore lipid nanoparticle delivery technology to develop a product candidate that is designed to specifically inhibit the gene HAO1, which encodes GO. We have generated highly potent and specific DsiRNAs targeting HAO1 and are now in the process of optimizing these DsiRNAs to enhance their pharmaceutical properties. We intend to complete this optimization in the first half of 2014 and declare a clinical candidate in this program. If successful, we would then seek to conduct manufacturing scale-up and Good Laboratory Practice (GLP) toxicity studies throughout 2014 in anticipation of initiating clinical trials in 2015.

We have packaged several DsiRNAs that showed activity in our tests targeting HAO1, which are not yet optimized, in a formulation of EnCore that efficiently delivers DsiRNAs to the mouse liver. Using these EnCore-formulated DsiRNAs targeting HAO1, we have observed up to 97 percent reduction of the HAO1 transcript in mouse liver after a single dose. We have used these same EnCore-formulated DsiRNAs targeting HAO1 in the animal model of PH1. In these treated mice we have observed a significant reduction in oxalate levels in the urine. In treated mice, the urinary oxalate levels are returned to near baseline levels, similar to normal mice. This result indicates that DsiRNAs targeting HAO1 can reduce the key pathology of PH1 in an animal model of PH1.

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Oxalate levels reduced from disease state to normal by Day 8

(DsiRNAs targeting HAO1 reduce urine oxalate in the animal model of PH1)

The graph shows the levels of urinary oxalate in mice that bear a genetic deletion of the gene encoding AGT1 after treatment with HAO1-1171 and HAO1-1378, which are DsiRNAs targeting HAO1, relative to saline control treated mice. In the absence of treatment, these mice have elevated urinary oxalate relative to normal mice. When these mice are treated only with saline control or with EnCore-formulated DsiRNAs targeting the Factor VII gene, their urinary oxalate remains elevated. When treated with DsiRNAs targeting HAO1, there is a significant reduction in urinary oxalate levels. DsiRNAs were injected on days 1, 4, 6, 10, and 14. Urine samples are collected to measure the accumulation of total oxalate excretion during a 24-hour period and are expressed as the mean +/- standard deviation.

95% Knockdown achieved and Gene Expression remains suppressed for at least 30 days

(Suppression of HAO1 mRNA expression by DsiRNA HAO1-1171 for at least 30 days)

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The graph shows the levels of mRNA encoding the protein glycolate oxidase in individual rodent livers after intravenous administration of a single dose of HAO1-1171 DsiRNA formulated in EnCore (Day 0). Relative to PBS-treated mice at Day 0, treatment with HAO1-1171 at 0.3 and 1.0 mg/kg reduced the target mRNA levels by 95% after one day, and continued to reduce mRNA levels by 50% and 75%, respectively, after 29 days.

Additional liver targets and programs under investigation

We are investigating a number of other rare diseases involving disease target genes expressed in the liver. In each case, we are evaluating the diseases and disease targets using a variety of criteria that include clinical need, applicability of our RNAi platform, feasibility of development, and market potential. Based on the investigation results, we could select one or more specific diseases or disorders to further research and develop.

DCR-M1711 in hepatocellular carcinoma (HCC)

We believe that our liver cancer product DCR-M1711 has the potential to be used in solid tumors from many tissues of origin, based on observed patterns of MYC amplification. This suggests a large potential market for DCR-M1711, depending upon its effectiveness. We have selected HCC as an initial focus indication for our MYC-related product candidate.

HCC accounts for 85 to 90 percent of primary liver cancers and represents a significant market opportunity for innovative therapeutics given the high unmet medical need in both established and developing markets. Liver cancer is the third leading cause of cancer-related deaths worldwide with over 695,000 annual deaths according to research published by the International Agency for Research on Cancer. Studies indicate that the annual HCC incidence rates are increasing and approximately 90,000 new patients are reportedly diagnosed each year in the seven major pharmaceutical markets (the U.S., France, Germany, Italy, Spain, the U.K. and Japan). Datamonitor Healthcare estimates that more than 414,000 HCC patients were diagnosed in the People s Republic of China (PRC) in 2013 and that the number of patients in the PRC will reach 496,600 in 2022, representing a 19.8 percent increase.

Therapeutic rationale for HCC and other MYC-related cancers

For several reasons, we have selected HCC as the initial indication for our MYC-targeted therapeutic. First, HCC patients frequently show amplifications of the MYC oncogene, suggesting a potentially important role for MYC activity in a significant fraction of HCC patients. Second, in animal models of disease, we have observed strong anti-tumor responses after treatments with our product candidate DCR-M1711. Finally, there are few therapies in development that directly target MYC.

Early-stage HCC is generally treated with surgery that has the potential to be curative. However, given the non-specific symptoms characteristic in HCC, the substantial majority of patients are diagnosed only after HCC is at an advanced stage. Advanced HCC has limited treatment options and is associated with poor patient outcome and high mortality. Chemotherapies have demonstrated poor efficacy in HCC and to our knowledge, there is no FDA approved chemotherapeutic regimen. Nexavar (marketed by Amgen Inc. and Bayer AG) is the only FDA approved therapeutic drug for the treatment of advanced or surgically unresectable HCC. Unmet medical needs include the identification and development of additional and more effective treatments for patients not eligible for surgical resection, a reduction in relapse rates and an increase in overall survival rates.

There is abundant evidence that the MYC oncogene is a driver of human cancer. The MYC oncogene, originally identified as a transformative agent in naturally-occurring tumor viruses, is one of the most frequently mutated oncogenes found in human cancers. A therapy that reduces or eliminates elevated MYC activity has the potential to

generate therapeutic benefits for patients with various tumor types that include MYC amplifications or other elevations of MYC activity. Inhibition of MYC activity has generated strong anti-tumor responses in a variety of animal models of cancer, which we have also observed in our own labs.

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Association of U.S. cancer patients with aberrant MYC expression

CANCER TYPE	APPROXIMATE PERCENTAGE OF PATIENTS
Liver (hepatocellular)	50%
Breast	80%
Colorectal	70%
Gastric	51-77%
Gynecological	90%
Prostate	80-90%
Small cell lung	18-30%

These mutations usually result in the duplication or higher-order amplification of the MYC oncogene with the tumor cell DNA, which is believed to result in elevated levels of MYC activity. Other types of mutations have also been shown to cause elevated levels of MYC activity such as chromosomal translocations that result in the activation of the MYC oncogene. In addition, human genetic variants known as single-nucleotide polymorphisms that are believed to predispose humans to cancers have been identified in MYC. Based on these genetic data in humans, we believe that a therapy that reduces or eliminates elevated MYC activity has the potential to generate therapeutic benefits for patients with various tumor types that include MYC amplifications or other elevations of MYC activity.

Supporting the potential for MYC-related therapy to be efficacious, inhibition of MYC activity has generated strong anti-tumor responses in a variety of animal models of cancer, which we have also observed in our own labs. Genetic techniques in mice, that reduce MYC expression or inhibit MYC protein activity, have been shown to prevent tumor formation or cause substantial tumor shrinkage, depending on the mouse genetic model of cancer employed in the experiment. These results have been obtained from mouse tumor models where MYC is not responsible for tumor initiation. We believe that these animal model data support the use of MYC-related therapy to treat cancer in humans.

Recent molecular work demonstrates that MYC over-expression drives the cancer process by selectively amplifying expression of genes typically expressed by a cell type. Based on this property, MYC is sometimes described as a universal amplifier, which can boost the activity of other cancer-related genes and push a cell to abnormal levels of growth. This model for MYC function suggests that an intervention that could bring down the expression of MYC to normal levels could have therapeutic benefit for cancer patients.

Despite its obvious attractiveness as a therapeutic target, we are not aware of any successful attempts to develop small molecule drugs that are active against MYC, and it is not a suitable target for antibody drugs because they cannot enter the interior of the cell, where MYC is located. A therapeutic agent that can reduce MYC expression is therefore still needed, and we believe that our platform has the potential to provide one.

Preclinical data for DCR-M1711

We have used our DsiRNA and EnCore lipid nanoparticle delivery technology to develop a product candidate that is designed to serve as a potent and specific inhibitor of the MYC oncogene. We have performed extensive screening and optimization of DsiRNAs targeting MYC, resulting in proprietary, potent, stable and non-immunostimulatory DsiRNAs that inhibit MYC in animal studies. We have packaged the DsiRNAs targeting MYC in a tumor-delivery formulation of EnCore that has exhibited the ability effectively to deliver DsiRNAs to multiple mouse tumor models,

including both xenograft models and a genetically-engineered mouse tumor model. The resulting product candidate that we have selected for development is known as DCR-M1711.

DCR-M1711 combines DsiRNAs targeting MYC with EnCore delivery technology. With DCR-M1711, we have shown a significant tumor response in mouse models of HCC.

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We have conducted extensive preclinical studies that have demonstrated that DCR-M1711 shows efficacy in tumor-bearing mice, while demonstrating tolerability in multiple animal species, including non-human primates. We have observed up to 70 percent reductions in the amount of the MYC oncogene transcript in xenograft-bearing mice models and similar strong reductions in MYC transcript level in a genetically engineered mouse tumor model. Based on these studies, we believe that DCR-M1711 has shown the properties that justify advancement into clinical development.

Anti-tumor efficacy of DCR-M1711 in a xenograft model of HCC

The graph shows the percentage reduction in final tumor volume in tumor-bearing mice treated with DCR-M1711 at the dose levels shown, compared to the tumors in saline control treated mice. This preclinical experiment indicates that DCR-M1711 treatment was effective in reducing the size of tumors. These mice have xenograft tumors of the human Hep3B HCC cell line in their livers, which were allowed to establish for 14 days prior to the commencement of dosing. Tumor-bearing mice were dosed with 5.0 to 0.5 milligrams per kilogram of DCR-M1711 or saline control administered intravenously three times per week for two weeks for a total of six doses.

Phase 1 clinical development plan for DCR-M1711

We intend to initiate a development program for DCR-M1711 that includes plans for two separate Phase 1 trials: one trial in patients with non-HCC tumors and one trial in patients with advanced HCC. Our plan is for each Phase 1 trial to be an open label study with two parts. The first part will be a standard dose escalation to determine the maximum tolerated dose in non-HCC patients. The second part will consist of an expansion cohort treated at the maximum tolerated dose. We submitted an IND application for DCR-M1711 for the treatment of HCC to the FDA in the first quarter of 2014 and have received from the FDA a non-objection letter to initiate the Phase 1 development.

Our first Phase 1 trial, which we expect to begin in the first half of 2014, has a primary objective of determining the safety and tolerability of DCR-M1711 in non-HCC patients and to determine the maximum tolerated dose when administered in a cycle of three weekly infusions followed by one week without an infusion. We plan to begin enrolling patients in this clinical trial at the South Texas Accelerated Research Therapeutics (START) in San Antonio, Texas. Additional trial sites may be added to the study during the dose escalation or expansion portions of the trial, if needed to meet enrollment goals.

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Our second Phase 1 trial, which we expect to begin in the second half of 2014, is planned to have a primary objective of determining the safety and tolerability of DCR-M1711 in patients with late stage HCC and to determine the maximum tolerated dose in these patients. We are evaluating where to begin enrolling patients in this trial and are likely to conduct this trial in the U.S. and in Asia.

As with most Phase 1 trials, ours will not be designed to yield statistically significant efficacy or molecular marker results. Accordingly, any observed results suggesting efficacy of DCR-M1711 may be due to chance and not to any effect of our drug candidate. The principal purpose of our Phase 1 trials will be to provide the basis for design of larger trials. Those trials will enroll more patients and they will be designed to demonstrate potential efficacy of the product candidate in a statistically significant way.

Product candidate for KRAS-related solid tumors

As a frequently-mutated oncogene that has historically been difficult to inhibit by the pharmaceutical industry, we believe that KRAS represents an excellent target for our RNAi-based therapy. We are pursuing DsiRNAs targeting KRAS in conjunction with our collaborator KHK. Under the terms of our collaboration, KHK is responsible for selecting the clinical product candidate, all preclinical and clinical development activities and the choice of patient population and disease indications for clinical trials. We have an option to co-promote in the U.S. for an equal share of the profits from U.S. net sales.

Activating mutations in the KRAS gene are commonly found in a wide variety of tumor types. Among cancer indications with large patient populations, KRAS is found to be mutated in approximately 90 percent of pancreatic cancers, approximately 40 percent of colorectal cancers and approximately 25 percent of non-small cell lung cancers. KRAS mutations are also found in cancers with smaller patient numbers, such as bile duct cancers. In general, the presence of a KRAS mutation correlates with poorer disease prognosis. In the case of non-small cell lung cancer, certain therapeutics approved by the FDA and other global regulatory agencies which have demonstrated clinical efficacy in non-small cell lung cancer are known to be ineffective in patients with KRAS mutations. While our collaborator KHK will decide which disease indications to pursue, we believe the potential market for a KRAS therapeutic could be significant. In the U.S. alone, there are estimated to be over 43,000 cases of pancreatic cancer, 125,000 cases of colorectal cancer and over 202,000 cases of non-small cell lung cancer diagnosed each year.

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Association of U.S. cancer patients with activating KRAS mutations

CANCER TYPE	APPROXIMATE PERCENTAGE WITH ACTIVATING KRAS MUTATIONS	IMPLIED PATIENT NUMBERS BASED ON INCIDENCE AND MUTATION FREQUENCY
Pancreatic adenocarcinoma	90%	38,700
Colorectal	40%	50,000
Non-small cell lung	25%	50,500

We believe that our DsiRNA for KRAS-related solid tumors could be developed and used with a companion diagnostic that allows for the selection of patients carrying tumors with KRAS mutations. Clinical diagnostic tests for the presence of KRAS mutations have already been approved by the FDA and other global regulatory agencies and are commercially available.

Therapeutic rationale for KRAS-related solid tumors

Historically, KRAS has been a difficult-to-inhibit driver oncogene target with a long history of studies indicating a high frequency of mutation in human tumors. To date, traditional small molecule approaches have not yielded successful drug candidates. Numerous studies have indicated that KRAS is a transformative agent in tumor viruses, which led to the identification of the human KRAS oncogene in the 1970s. Furthermore, similar to MYC, KRAS is mutated at high frequency in a number of human tumors, including some of the most prevalent tumor types in the established tumor markets.

In its normal, non-mutant form, the KRAS protein plays a key role in the promotion and regulation of cell growth and division. The KRAS protein acts in a keystone position in an intracellular signaling pathway often called the Ras-MAP Kinase pathway. This pathway is responsible for receiving growth-promoting signals from outside the cell and communicating those signals within the cell so that the cell can respond appropriately to the cell growth signals.

Preclinical data for product candidate for KRAS-related solid tumors

KRAS was the initial target of our December 2009 collaboration with KHK. During the first two years of the collaboration, KHK and our scientists worked to identify optimal DsiRNAs against the KRAS oncogene and to optimize the delivery technology containing KHK s proprietary lipids for tumor delivery. These DsiRNAs and formulations were tested both in cell culture and in animals using human tumor cell lines, from different tumor types, carrying activating mutations in the KRAS oncogenes.

Full tumor regression shown in the KRAS-positive pancreatic tumor model MIA PaCa-2

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Xenograft tumors were grown subcutaneously in mice, followed by intravenous treatment with KRAS associated cancer product candidate. Treated animals showed full tumor regression, while saline control treated animals showed rapid tumor growth.

The KRAS DsiRNAs and formulations have shown activity in both cell culture and xenograft animal tumor models. For example, full regression of subcutaneous xenograft pancreatic tumors can be achieved with KRAS DsiRNAs. These results were independently generated at our facility in Massachusetts and at KHK s facility in Japan and have been observed using five independent KRAS sequences. Additional controls appear to rule out the activity of any residual immunologic activity in the mice. Taken together, these data strongly suggest that the tumor response is due to the KRAS DsiRNA. As expected, KRAS oncogene knockdown is observed in tumors after a single dose of KRAS DsiRNA, further validating the assumption of efficacy.

Based on these preclinical efficacy data, KHK has advanced a compound resulting from this program into development. KHK has assumed responsibility for preclinical and clinical development of the program and bears the expense of that effort.

We are also developing a product candidate targeting an oncogene in collaboration with KHK. In January 2013, we announced that KHK elected to advance this second therapeutic oncology product candidate from the research to the development stage. The achievement of this milestone triggered a $5.0 million payment from KHK to us. KHK is responsible for all development costs associated with this product candidate and has worldwide commercialization rights. We are eligible to receive royalties on worldwide net sales of the product candidate.

Strategic Partnerships and Collaborations

KHK research collaboration and license agreement

In December 2009, we entered into a research collaboration and license agreement (the collaboration agreement) with KHK for the research, development and commercialization of drug delivery platforms and DsiRNA molecules for therapeutic targets, primarily in oncology. Under the collaboration agreement, we engaged in the discovery of DsiRNA molecules against KRAS and other gene targets nominated by KHK. In 2011, KHK exercised its option for one additional target, the identity of which has not been publicly disclosed. As part of the research we are conducting in the collaboration, we are using our specific RNAi-inducing double-stranded DsiRNA molecules with a lipid nanoparticle drug delivery platform proprietary to KHK. KHK is responsible for all costs it incurs to develop any compound that is directed against a target included in the collaboration that KHK designates for development, subject to our exercise of our co-promotion option with respect to that compound if that compound is directed against KRAS.

We have granted KHK an exclusive license in 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.

Under the terms of the collaboration agreement, we have received total payments of $17.5 million. We are entitled to receive up to an additional $110.0 million for each product candidate resulting from the collaboration of certain clinical, regulatory and commercialization milestones. KHK is also obligated to pay us royalties on net sales of products resulting from the research collaboration. These royalties vary depending on the total net sales and range from percentages of net sales in the high single digits to the teens. None of the previously paid milestones are subject to reimbursement.

We have the option to elect to co-promote the oncogene KRAS product in the U.S. for an equal share of the profits resulting from U.S. net sales of the product.

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If we exercise our option to co-promote an oncogene KRAS product in the U.S., the collaboration agreement will remain in effect pursuant to its terms in the U.S. for as long as any product is being sold by either KHK or us in the U.S. For each country outside of the U.S., the agreement will remain in effect pursuant to its terms on a product-by-product and country-by-country basis until the later of the last to expire of any patent rights licensed under the agreement applicable to the manufacture, use or sale of the product or twelve years after the date of the first commercial sale of such product in the applicable country. In the event we do not exercise our option to co-promote an oncogene KRAS product in the U.S., the collaboration agreement will remain in effect pursuant to its terms on a product-by-product and country-by-country basis until the later of the last to expire of any patent rights licensed under the agreement applicable to the manufacture, use or sale of the product or twelve years after the date of the first commercial sale of such product in the applicable country.

KHK may terminate the agreement at any time upon prior written notice to us. We may terminate the agreement if KHK challenges the validity or enforceability of any patents licensed by us to KHK. Either we or KHK may terminate the agreement in the event of the bankruptcy or uncured material breach by the other party. Finally, KHK may terminate the agreement in its entirety at the end of the research collaboration if it determines not to proceed with further development of compounds.

City of Hope license agreement

In September 2007, we entered into a license agreement with City of Hope (COH), an academic research and medical center, pursuant to which COH has granted to us an exclusive (subject to the exception described below), royalty-bearing, worldwide license under certain patent rights in relation to DsiRNA, including the core DsiRNA patent (U.S. 8,084,599), to manufacture, use, offer for sale, sell and import products covered by the licensed patent rights for the prevention and treatment of any disease in humans. COH is restricted from granting any additional rights to develop, manufacture, use, offer to sell, sell or import products covered by the licensed patent rights for the prevention and treatment of any disease in humans. Prior to entering into the license with us, COH had entered into a non-exclusive license 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 that non-exclusive license has been terminated, 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 Research Corporation, as successor to the non-exclusive license holder. In addition, COH has granted to us an exclusive, royalty-bearing, worldwide license under the licensed patent rights providing certain rights for up to 20 licensed products selected by us for human diagnostic uses, provided that COH has not granted or is not negotiating a license of rights to diagnostic uses for such licensed products to a third party. The exclusive licenses granted by COH to us under the agreement are subject to any retained rights of the U.S. government in the licensed patent rights and a royalty-free right of COH to practice the licensed patent rights for educational, research and clinical uses. We have the right to sublicense the licensed patent rights to third parties with COH s written consent. The core DsiRNA patent (U.S. 8,084,599), titled methods and compositions for the specific inhibition of gene expression by double-stranded RNA, describes RNA structures having a 25 to 30 nucleotides sense strand, a blunt end at the 3 end of the sense strand and a one to four nucleotides overhang at the 3 end of the antisense strand. The expiration date of this patent is July 17, 2027.

Pursuant to the terms of the agreement, we paid COH a one-time, non-refundable license fee and issued shares of our common stock to COH and a co-inventor of the core DsiRNA patent. COH is entitled to receive milestone payments in an aggregate amount of up to $5.25 million for each licensed product upon achievement of certain clinical and regulatory milestones. COH is further entitled to receive royalties at a low single-digit percentage of any net sale revenue of the licensed products sold by us and our sublicensees. If we sublicense the licensed patent rights to a third party, COH has the right to receive a double digit percentage of sublicense income, the percentage of which decreases

after Dicerna has expended $12.5 million in development and commercialization costs. We are also obligated to pay COH an annual license maintenance fee, which may be credited against any royalties due to COH in the same year, and reimburse COH for expenses associated with the

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prosecution and maintenance of the license patent rights. Royalties shall be paid on a product-by-product and country-by-country basis until the expiration in each country of the last to expire of the licensed patent rights.

Under the agreement, we are obligated to use commercially reasonable efforts to develop and commercialize the licensed products in certain major markets. COH has the right to terminate the agreement in its entirety if we fail to enroll patients for clinical trials of one or more licensed products at various phases before certain specified deadlines unless we exercise the right to extend the deadlines in one-year increments by making a payment of $0.5 million to COH for each one-year extension. We have extended one milestone deadline for three one-year extensions, paying an aggregate of $1.5 million to COH for such extensions.

The agreement will remain in effect pursuant to its terms until all of the obligations under the 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 agreement upon our bankruptcy or insolvency. We may terminate the agreement without cause upon written notice to COH.

Intellectual Property

We invest significant amounts in research and development. Our research and development expenses were approximately $10.7 million, $11.6 million and $11.6 million in 2011, 2012 and 2013, 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 three U.S. patents and a number of pending patent applications with claims to methods and compositions of matters that cover various aspects of our RNAi technology and our discovery technologies, including our proprietary DsiRNA molecules and lipid delivery vehicles. Our three U.S. patents are U.S. 8,349,809 (issued in January 2013 with an expiration date of January 2030), U.S. 8,372,816 (issued in February 2013 with an expiration date of April 2030) and U.S. 8,513,207 (issued in August 2013 with an expiration date of May 2030). We also own numerous patent applications covering specific DsiRNA sequences that drive activity against high value disease targets, including MYC, KRAS, CTNNB1 (ß-catenin), and other targets. Further, we own seven U.S. patents expiring between 2015 and 2017 and numerous patent applications with claims to methods and compositions of matters related to our lipid delivery technology, such as lipid compositions and particle formulations and the EnCore formulation process. We have issued or pending claims to DsiRNA 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. Depending on the subject matter of future issued claims, we may also jointly own 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 worldwide patent coverage with a focus on jurisdictions that represent significant global pharmaceutical markets. Generally, patents have a term of twenty years from the earliest priority date, assuming that all maintenance

fees are paid, no portion of the patent has been terminally disclaimed and the patent has not

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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.

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 can be costly and time consuming. Issued patents can be subject to oppositions, interferences and other third party challenges that can result in the revocation of the patent 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 has expired or will be in force for only a short period of time following commercialization. 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 partners 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 partners 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.

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 the company 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 the property of the company. 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.

In-licenses

In addition to the license agreement with COH described above, we have entered into license agreements for RNA technology that may benefit us as we advance our programs.

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Plant Bioscience Limited license agreement

In September 2013, we entered into a commercial license agreement with Plant Bioscience Limited (PBL), pursuant to which PBL has granted to us a nominated-target-limited, worldwide, non-exclusive, fee-bearing license to certain of its U.S. patents (the Baulcombe patent estate) and patent applications to research, discover, develop, manufacture, sell, import and export, for human diagnostic and therapeutic uses, products incorporating one or more short RNA molecules (SRMs) designed to target and modify the expression of a human gene or genes nominated by us from time to time. We are entitled to nominate multiple SRMs and have so far nominated one gene as the first SRM under the agreement. We are not obligated to nominate any additional genes.

We have paid PBL a one-time, non-refundable signature fee and will pay PBL a nomination fee for any additional SRMs nominated by us under the agreement. We are further obligated to pay PBL milestone payments in an aggregate amount of up to $3.85 million for each licensed product upon achievement of certain clinical and regulatory milestones. In addition, PBL is entitled to receive royalties at a low single-digit percentage of any net sale revenue of any licensed products sold by us. The agreement will expire on a country-by-country basis in each country where any licensed products are used, provided, manufactured or sold upon the date of the last to expire of applicable valid claim. Each party may terminate the agreement for any uncured material breach by the other party. We may terminate the agreement at any time for convenience upon prior written notice to PBL.

Carnegie Institution of Washington license agreement

In January 2009, we entered into a license agreement with the Carnegie Institution of Washington (Carnegie), pursuant to which Carnegie has granted to us a worldwide, non-exclusive license under certain of its patents and patent applications (the Fire and Mello patent estate) relating to genetic inhibition by double-stranded RNA molecules for internal research, screening and development of product candidates for human and non-human diagnostic and therapeutic uses. We have paid Carnegie a one-time upfront fee and will in addition pay an annual license fee during the term of the agreement. We are further obligated to make two one-time additional payments in the aggregate amount of $100,000 upon achievement of the filing with the FDA of an NDA for a licensed product candidate and the first commercial sale of a licensed product candidate or licensed method. Carnegie is entitled to receive royalties on any net sale revenue from licensed product candidates sold by us, with the royalty rate to be further negotiated between Carnegie and us in good faith reflecting customary rates in the industry.

The agreement will terminate with respect to each licensed product candidate upon the last to expire of any valid claim within the licensed patent rights. Each party may terminate the agreement upon any uncured material breach by the other party. We may terminate the agreement at any time for any reason upon written notice to Carnegie.

Manufacturing and Supply

We do not currently own or operate manufacturing facilities for the production of preclinical, clinical or commercial quantities of any of our product candidates. We currently contract with only one drug product formulation manufacturer for the encapsulation of the oligonucleotide in a lipid nonparticle and we expect to continue to do so to meet the preclinical and any clinical requirements of our product candidates. We do not have a long term agreement with this third party.

Currently, each 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.

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KHK is responsible for all manufacturing under our collaboration agreement with KHK both for the KRAS DsiRNA and the oncology program selected by KHK for development under the agreement.

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, have fewer side effects, 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 DsiRNAs for therapeutic use. However, there are several companies that are currently developing RNAi-based therapies for various indications. Among these, Alnylam Pharmaceuticals, Inc. (Alnylam) in partnership with Genzyme (a Sanofi company) is developing its ALN-TTR program, which is an RNAi-based therapy for the treatment of transthyretin-mediated amyloidosis (ATTR) and is currently in Phase 3 trials. Alnylam is also developing RNAi-based Alnylam therapies for other indications, including hemophilia, porphyria, hypercholesterolemia, hemoglobinopathies, and alpha-1-antitrypsin (AAT) deficiency hepatocyte, inclusions, among others. In January 2014, Alnylam and Genzyme entered into a collaboration to expand their partnership, under which Genzyme acquired significant global rights to Alnylam s pipeline outside of North America and Western Europe where Alnylam retains most product rights after the collaboration became effective in February 2014. Genzyme also became a major shareholder in Alnylam by making a $700 million equity investment in Alnylam. Tekmira Pharmaceuticals Corporation is developing its TKM-PLK1 for solid tumors and is currently in Phase 1/2 studies for gastrointestinal neuroendocrine tumors (GI-NET) and adrenocortical carcinoma (ACC). Tekmira also is clinically investigating its RNAi molecules for use in treating Ebola virus, hepatitis B (HBV), alcohol use disorder as well as other preclinical programs. Tekmira has rights under Alnylam s intellectual property to develop thirteen RNAi therapeutic products. Additionally, Arrowhead Research Corporation is developing ARC-520 for chronic hepatitis B and announced in March 2014 the advancement of this program into a Phase 2a clinical trial. Quark Pharmaceuticals, Inc. is in a partnership with Pfizer for the development of PF-655 for diseases of the eye and is in Phase 2 studies. Quark is also partnered with Novartis for the development of QPI-1002 and granted Novartis an option for a worldwide exclusive license to the product candidate for all indications.

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In addition to RNAi therapies, there are other intracellular technologies focused on silencing the activity of specific genes by targeting RNAs copied from them. Companies such as miRagen Therapeutics, Inc., Mirna Therapeutics, Inc., Regulus Therapeutics Inc. and Santaris Pharma A/S target or utilize microRNAs, which are 15 to 22 nucleotide, short, non-coding RNAs, to alter mRNA expression levels. The product candidates being developed by these companies are currently in preclinical and clinical trials for various indications. Isis Pharmaceuticals, Inc. markets and develops antisense therapies, 12 to 21 nucleotide, synthetic DNA- or RNA-like compounds, for a range of indications. Isis drug KYNAMRO (partnered with Sanofi) is marketed as an adjunct to lipid-lowering medications in patients with homozygous familial hypercholesterolemia (HoFH) and Isis is seeking additional indications for the product.

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

Hepatocellular Carcinoma (HCC)

There are limited treatments for HCC in the U.S. and abroad. If diagnosed as early-stage HCC, the disease is generally treated with surgical resection of the liver and has the potential to be curative. The vast majority of patients diagnosed with HCC, however, are in the advanced stages, for which chemotherapies have demonstrated poor efficacy. To our knowledge, there is no FDA-approved chemotherapeutic regimen. Nexavar is the only effective drug for the treatment of advanced or unresectable HCC in our belief. Given the high unmet medical need and the commercial success of Nexavar, numerous targeted therapies for the treatment of hepatocellular carcinoma (HCC) are under development. Targeted therapies represent the largest proportion of the HCC pipeline.

Primary Hyperoxaluria 1 (PH1)

The current standard of care for treating PH1 is dual-organ transplant, namely a kidney and liver transplant in patients with PH1, 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. To our knowledge, there are no therapies for the treatment of PH1, either marketed or in clinical development, with evidence of significant clinical benefit and impact on disease progression.

Solid tumors

There are a number of pharmaceuticals and biologics that are marketed or in clinical development for the treatment of solid tumors. The most common treatments for solid tumors are various chemotherapeutic agents, radiation therapy and certain targeted therapies, including monoclonal antibodies such as Avastin, Erbitux, Herceptin and Vectibix. Small molecules, such as Nexavar, Sutent and Tarceva, are also indicated for the treatment of solid tumors. In contrast, our proprietary DsiRNA molecules target tumors in which there is overexpression of the MYC and KRAS oncogenes. To our knowledge, only one small molecule (salirasib (KD032)) is being evaluated by Kadmon Corporation, LLC in clinical trials for the treatment of KRAS-specific non-small cell lung cancer, pancreatic cancer and other solid tumors. Additionally, we are not aware of any clinical trial that is currently evaluating a therapy for the treatment of solid tumors in which the MYC oncogene is specifically targeted.

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, labeling, packaging, promotion, storage, advertising, distribution, marketing 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

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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.

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 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;
- warning letters;
- product seizures;
- total or partial suspension of production or distribution; or
- injunctions, fines, disgorgement, or civil or criminal penalties.

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

- completion of nonclinical laboratory tests, animal studies and formulation studies conducted according to Good Laboratory Practices (GLPs) or other applicable regulations;
- submission to the FDA of an IND application, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to Good Clinical Practices (GCPs) to establish the safety and efficacy of the product candidate for its intended use;

submission to the FDA of an NDA;

satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product candidate is produced to assess compliance with current Good Manufacturing Practices (cGMPs) to assure that the facilities, methods and controls are adequate to preserve the product candidate s identity, strength, quality and purity; 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, 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.

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All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCPs. 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 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 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. An institutional review board (IRB) at each institution participating in the clinical trial must review and approve the protocol before a clinical trial commences at that institution and must also approve the information regarding the trial and the consent form that must be provided to each research subject or the subject s legal representative, monitor the study until completed and otherwise comply with IRB regulations.

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 or the sponsor 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. These points may be 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 the new drug. 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 (SPA), 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 quality, purity and potency of the

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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.

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. NDAs receive either standard or priority review. A drug representing a significant improvement in treatment, prevention or diagnosis of disease may receive priority review. 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 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 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. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured and tested.

Expedited review and approval

The FDA has various programs, including Fast Track, priority review and accelerated approval, which are intended to expedite or simplify the process for reviewing product candidates, or provide for the approval of a product candidate on the basis of a surrogate endpoint. 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. 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. For example, Fast Track is a process designed to facilitate the development and expedite the review of product candidates to treat serious or life-threatening diseases or conditions and fill unmet medical needs. Priority review is designed to give product candidates that offer major advances in treatment or provide a treatment where no adequate therapy exists an initial review within six months as compared to a standard review time of ten months.

Although Fast Track and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track designated product candidate and expedite review of the application for a product candidate designated for priority review. Accelerated approval, which is described in Subpart H of 21 CFR Part 314, provides for an earlier approval for a new product candidate that is intended to treat a serious or life-threatening disease or condition and that fills an unmet medical need based on a surrogate endpoint. A surrogate endpoint is a laboratory measurement or physical sign used as an indirect or substitute measurement representing a clinically meaningful outcome. As a condition of approval, the FDA may require that a sponsor of a product candidate receiving accelerated approval perform post-marketing clinical trials.

In the Food and Drug Administration Safety and Innovation Act (FDASIA), which was signed into law in July 2012, the U.S. Congress encouraged the FDA to utilize innovative and flexible approaches to the assessment of product candidates under accelerated approval. The law required the FDA to issue related draft guidance within a year after the law s enactment and also promulgate confirming regulatory changes. In June 2013, the

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FDA published a draft Guidance for Industry titled Expedited Programs for Serious Conditions Drugs and Biologics, which provides guidance on FDA programs that are intended to facilitate and expedite development and review of new product candidates as well as threshold criteria generally applicable to concluding that a product candidate is a candidate for these expedited development and review programs.

In addition to the Fast Track, accelerated approval and priority review programs discussed above, the FDA also provided guidance on a new program for Breakthrough Therapy designation. The FDA defines a Breakthrough

Therapy as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and 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 drug designated as a Breakthrough Therapy is eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a Breakthrough Therapy. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. A request for Breakthrough Therapy designation should be submitted concurrently with, or as an amendment to an IND. FDA has already granted this designation to approximately 30 new product candidates and recently approved the first Breakthrough Therapy designated drug.

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 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

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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 to market the same product candidate for the same indication, except in very limited circumstances, for seven years. Orphan drug exclusivity, however, could also block the approval of one of our product candidates for seven years if a competitor obtains approval of the same product candidate as defined by the FDA or if our product candidate is determined to be contained within the competitor s product candidate for the same indication or disease.

Pediatric exclusivity and pediatric use

Under the Best Pharmaceuticals for Children Act (BPCA), 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.

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 application 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 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.

As part of the FDASIA, the U.S. Congress made a few revisions to BPCA and PREA, which were slated to expire on December 31, 2012, and made both laws permanent.

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. Later

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discovery of previously unknown problems with a product candidate may result in restrictions on the product candidate 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 claims, 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;
- providing the FDA with updated safety and efficacy information;
- drug sampling and distribution requirements;
- notifying the FDA and gaining its approval of specified manufacturing or labeling changes; and
- complying with FDA promotion and advertising requirements.

Drug manufacturers and other entities involved in the manufacture and distribution of approved product candidates are required to register their establishments with 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 countries 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 economic areas, such as the European Union, 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 European Union regulatory systems, a company may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure, which is compulsory for medicines produced by biotechnology or those medicines intended to treat AIDS, cancer, neurodegenerative disorders or diabetes and is optional for those medicines which are highly innovative, provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized 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 assessments report, each member state must decide whether to recognize 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 European Union before the application for marketing authorization is made. Orphan drugs in Europe enjoy economic and marketing benefits, including up to ten years of market exclusivity for the approved indication unless another applicant can show that its product is safer, more effective or otherwise clinically superior to the orphan-designated product.

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Reimbursement

Sales of our products will depend, in part, on the extent to which the costs of our products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. These 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. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and 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 American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research will be developed by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures will be made to the U.S. Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of any product, if any such product or the condition that it is intended to treat is the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits in a competitor s product could adversely affect the sales of our product candidates. If third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products 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 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, is expected to have a significant impact on the health care industry. ACA is expected to expand coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, among other things, ACA is expected to expand and increase industry rebates for drugs covered under Medicaid programs and make changes to the

coverage requirements under the Medicare Part D program. We cannot predict the impact of ACA on pharmaceutical companies, as many of the ACA reforms require the promulgation of

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detailed regulations implementing the statutory provisions which has not yet occurred. In addition, although the U.S. Supreme Court upheld the constitutionality of most of the ACA, some states have indicated that they intend to not implement certain sections of the ACA, and some members of the U.S. Congress are still working to repeal parts of the ACA. These challenges add to the uncertainty of the legislative changes enacted as part of ACA.

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 European Union 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 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 European Union do not follow price structures of the U.S. and generally tend to be significantly lower.

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 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 and the ability to negotiate acceptable commercial terms with third parties.

Scientific Advisors

We seek advice from our scientific advisory board, which consists of a number of leading scientists and physicians, on scientific and medical matters. Our scientific advisory board meets periodically to assess:

- our research and development programs;
- the design and implementation of our clinical programs;

our patent and publication strategies;

new technologies relevant to our research and development programs; and

specific scientific and technical issues relevant to our business.

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The current members of our scientific advisory board are as follows.

NAME	POSITION AND INSTITUTIONAL AFFILIATION
Mark Behlke, M.D., Ph.D.	Chief Scientific Officer, Integrated DNA Technologies
Frank McCormick, Ph.D., F.R.S., D.Sc. (Hon)	Director, University of California, San Francisco Helen Diller Family Comprehensive Cancer Center
Joseph Bonventre, M.D., Ph.D.	Director, Renal Division, Samuel A. Levine Professor of Medicine, Brigham and Women s Hospital, Harvard Medical School
John Rossi, Ph.D.	Co-Founder of Dicerna and Professor and Dean of Irell and Manella Graduate School of Biological Sciences at City of Hope s Beckman Research Institute

Employees

As of December 31, 2013, we had 22 full-time employees, of whom 16 are engaged in research and development and six in administration. None of our employees is represented by a labor union or covered by a collective bargaining agreement. Geographically, all employees are located in Massachusetts. We consider our relationship with our employees to be good.

Initial Public Offering

On February 4, 2014, we closed the initial public offering of our common stock, in which we sold an aggregate of 6,900,000 shares of common stock, including 900,000 shares sold pursuant to the exercise in full by the underwriters of an option to purchase additional shares, at an offering price of $15.00 per share, before deducting underwriting commissions and discounts. The aggregate net proceeds to us were approximately $92.9 million, after deducting underwriting commissions and discounts and the offering expenses payable by us. Jefferies LLC, Leerink Partners LLC, and Stifel, Nicolaus & Company, Incorporated acted as joint book-running managers for the initial public offering. Robert W. Baird & Co. Incorporated acted as co-lead manager for the initial public offering.

Corporate Information

We were incorporated in Delaware in 2006. We maintain our executive offices at 480 Arsenal Street, Building 1, Suite 120, Watertown, Massachusetts 02472, and our main telephone number is (617) 621-8097. Our website is located at 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, this Annual Report on Form 10-K.

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 $1.0 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.

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Our website address is *http://www.dicerna.com*. 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 Securities Exchange Commission (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*.

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Item 1A. *Risk Factors*

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

Risks Related to Our Business

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

We are a preclinical stage biopharmaceutical company with a limited operating history, focused on the discovery and development of treatments based on the emerging therapeutic modality RNA interference (RNAi), a biological process in which ribonucleic acid (RNA) molecules inhibit gene expression. Since our inception in October 2006, we have devoted our resources to the development of Dicer substrate RNA (DsiRNA) molecules and delivery technologies. We have had significant operating losses since our inception. As of December 31, 2013, we had an accumulated deficit of $85.5 million. For the twelve months ended December 31, 2011, 2012 and 2013, our net loss was $8.6 million, $10.1 million and $18.5 million, respectively. Substantially all of our losses have resulted from expenses incurred in connection with our research programs and from general and administrative costs associated with our operations. Our technologies and product candidates are in early stages of development, and we are subject to the risks of failure inherent in the development of product candidates based on novel technologies.

To date, we have generated revenue primarily from the receipt of upfront research funding, license and option exercise fees and preclinical payments under our research collaboration and license agreement with Kyowa Hakko Kirin Co., Ltd. (KHK). We have not generated, and do not expect to generate, any product revenue 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 collaborator, 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 collaborator, 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.

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

In December 2009, we entered into a research collaboration and license agreement with KHK for the research, development and commercialization of DsiRNA molecules and drug delivery technologies for therapeutic targets, primarily in oncology. Under the research collaboration and license agreement with KHK,

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KHK has paid us a total of $17.5 million as of December 31, 2013. During the first two years of the collaboration, we worked together with KHK to optimize KHK s lipid nanoparticles for tumor delivery and to identify DsiRNAs optimized against oncology and KRAS targets. Based on the results of this research, KHK exercised options to advance two separate DsiRNAs into the development stage, including one with a KRAS target. For each product candidate under the research collaboration and license agreement, we have the potential to receive clinical, regulatory and commercialization milestone payments of up to $110.0 million and royalties on net sales of such product candidate. The success of our collaboration programs with KHK depends entirely upon the efforts of KHK. Except for certain co-promotion and profit sharing rights we retain with respect to the KRAS product candidate if it is approved for marketing and commercialization in the U.S., KHK has sole discretion in determining and directing the efforts and resources, including the ability to discontinue all efforts and resources, it applies to the development and, if approval is obtained, commercialization and marketing of the product candidates covered by the collaboration. KHK may not be effective in obtaining approvals for the product candidates developed under the collaboration arrangement or in marketing, or arranging for necessary supply, manufacturing or distribution relationships for, any approved products. Under the research collaboration and license agreement, KHK may change its strategic focus or pursue alternative technologies in a manner that results in reduced, delayed or no revenue to us. KHK has a variety of marketed products and product candidates under collaboration with other companies, including some of our competitors, and its own corporate objectives may not be consistent with our best interests. If KHK fails to develop, obtain regulatory approval for or ultimately commercialize any product candidate under our collaboration or if KHK terminates our collaboration, our business, financial condition, results of operations and prospects could be materially and adversely affected. In addition, any dispute or litigation proceedings we may have with KHK in the future could delay development programs, create uncertainty as to ownership of intellectual property rights, distract management from other business activities and generate substantial expense.

We will need 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.

If our product candidates enter and advance through preclinical studies and clinical trials, we will need substantial additional funds to expand our development, regulatory, manufacturing, marketing and sales capabilities or contract with other organizations to provide these capabilities for us. We have used substantial funds to develop our product candidates and delivery technologies and will require significant funds to conduct further research and development and preclinical testing and clinical trials of our product candidates, to seek regulatory approvals for our product candidates and to manufacture and market products, if any, that are approved for commercial sale. As of December 31, 2013, we had $46.6 million in cash, cash equivalents and short-term investments. In addition, we received approximately $92.9 million of net proceeds, after deducting the underwriting commissions and discounts and the offering expenses payable by us, from the initial public offering of 6,900,000 shares of our common stock closed on February 4, 2014. Based on our current operating plan, we believe that our available cash, cash equivalents and short-term investments, the net proceeds from the initial public offering and available borrowings under our credit facility, will be sufficient to fund our anticipated level of operations through 2016. Our future capital requirements and the period for which we expect our existing resources to support our operations may vary significantly from what we expect. Our monthly spending levels vary based on new and ongoing development and corporate activities. Because the length of time and activities associated with successful development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. To execute our business plan, we will need, among other things:

to obtain the human and financial resources necessary to develop, test, obtain regulatory approval for, manufacture and market our product candidates;

to build and maintain a strong intellectual property portfolio and avoid infringing intellectual property of third parties;

to establish and maintain successful licenses, collaborations and alliances;

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to satisfy the requirements of clinical trial protocols, including patient enrollment;

to establish and demonstrate the clinical efficacy and safety of our product candidates;

to obtain regulatory approvals;

to manage our spending as costs and expenses increase due to preclinical studies and clinical trials, regulatory approvals and commercialization;

to obtain additional capital to support and expand our operations; and

to market our products to achieve acceptance and use by the medical community in general.

If we are unable to obtain funding on a timely basis or on acceptable terms, we may have to delay, reduce or terminate our research and development programs and preclinical studies or clinical trials, if any, limit strategic opportunities or undergo reductions in our workforce or other corporate restructuring activities. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies or product candidates that we would otherwise pursue on our own. We do not expect to realize revenue from product sales, milestone payments or royalties in the foreseeable future, if at all. Our revenue sources are, and will remain, extremely limited unless and until our product candidates are clinically tested, approved for commercialization and successfully marketed. To date, we have primarily financed our operations through the sale of securities, debt financings, credit and loan facilities and payments received under our collaboration and license agreement with KHK. We will be required to seek additional funding in the future and intend to do so through either collaborations, equity offerings or debt financings, credit or loan facilities or a combination of one or more of these funding sources. Our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. Additional funds may not be available to us on acceptable terms or at all. If we raise additional funds by issuing equity securities, our stockholders will suffer dilution and the terms of any financing may adversely affect the rights of our stockholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Debt financing, if available, may involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of equity securities received any distribution of corporate assets.

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 collaborator or any future collaborator or licensing partner;

the timing of the release of results from any clinical trials conducted by us or our collaborator KHK;

our execution of any collaboration, licensing or similar arrangement, and the timing of payments we may make or receive under such existing or future arrangements or the termination or modification of any such existing or future arrangements;

any intellectual property infringement lawsuit or opposition, interference or cancellation proceeding in which we may become involved;

additions and departures of key personnel;

strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;

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if any of our product candidates receives regulatory approval, market acceptance and demand for such product candidates;

regulatory developments affecting our product candidates or those of our competitors; and

changes in general market and economic conditions.

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

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

We plan to develop a pipeline of product candidates using our DsiRNA molecules and delivery technologies for rare inherited diseases involving the liver and cancers that are genetically defined. We believe that product candidates identified with our drug discovery and delivery platform may offer an improved therapeutic approach to small molecules and monoclonal antibodies, as well as several advantages over earlier generation RNAi molecules. However, the scientific research that forms the basis of our efforts to develop product candidates based on the therapeutic modality RNAi and the identification and optimization of DsiRNA is relatively new. Further, the scientific evidence to support the feasibility of developing therapeutic treatments based on RNAi and DsiRNA 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 DsiRNA does not possess certain properties required for a drug to be effective, such as the ability to remain stable in the human body for the period of time required for the drug to reach the target tissue or the ability to cross the cell wall and enter into cells within the target tissue for effective delivery. We currently have only limited data, and no conclusive evidence, to suggest that we can introduce these necessary drug-like properties into DsiRNA. We may spend substantial funds attempting to introduce these properties and may never succeed in doing so. In addition, product candidates based on DsiRNA may demonstrate different chemical and pharmacological properties in patients than they do in laboratory studies. Even if product candidates, such as DCR-PH1 and DCR-M1711, 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 U.S. Food and Drug Administration (FDA) has relatively limited experience with RNAi and DsiRNA based therapeutics. No regulatory authority has granted approval to any person or entity, including us, to market and commercialize therapeutics using RNAi or DsiRNA, which may increase the complexity, uncertainty and length of the regulatory approval process for our product candidates. We and our current collaborator, 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 DsiRNA

prove to be ineffective, unsafe or commercially unviable, our entire platform and pipeline would have little, if any, value, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

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

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

With our focus on the emerging therapeutic modality RNAi, these risks may increase to the extent the space becomes more competitive or less favored in the commercial marketplace. Additional risks apply in relation to any disease

indications we pursue which are classified as rare diseases and allow for orphan drug designation by regulatory agencies in major commercial markets, such as the U.S., Europe and Japan. For instance, we are in the preliminary stages of developing a treatment for the rare genetic disorder Primary Hyperoxaluria 1 (PH1) with the gene encoding the liver metabolic enzyme glycolate oxidase as our target. Because of the small patient population for a rare disease, if pricing is not approved or accepted in the market at an appropriate level for an approved product with orphan drug designation, such drug may not generate enough revenue to offset costs of development, manufacturing, marketing and commercialization despite any benefits received from the orphan drug designation, such as market exclusivity, assistance in clinical trial design or a reduction in user fees or tax credits related to development expense. Market size is also a variable in disease indications not classified as rare. Our estimates regarding potential market size for any indication may be materially different from what we discover to exist at the time we commence commercialization, if any, for a product, which could result in significant changes in our business plan and have a material adverse effect on our business, financial condition, results of operations and prospects.

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

We have no products on the market and all of our product candidates are in early stages of development. Our ability to achieve and sustain profitability depends on obtaining regulatory approvals, including institutional review board (IRB) approval, for and successfully commercializing our product candidates, either alone or with third parties, such as our collaborator KHK. Before obtaining regulatory approval for the commercial distribution

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of our product candidates, we or a collaborator must conduct extensive preclinical tests and clinical trials to demonstrate the safety and efficacy in humans of our product candidates. Preclinical testing and clinical trials are expensive, difficult to design and implement, can take many years to complete and are uncertain as to outcome. The start or end of a clinical study is often delayed or halted due to changing regulatory requirements, manufacturing challenges, required clinical trial administrative actions, slower than anticipated patient enrollment, changing standards of care, availability or prevalence of use of a comparative drug or required prior therapy, clinical outcomes or financial constraints. For instance, delays or difficulties in patient enrollment or difficulties in retaining trial participants can result in increased costs, longer development times or termination of a clinical trial. Clinical trials of a new product candidate require the enrollment of a sufficient number of patients, including patients who are suffering from the disease the product candidate is intended to treat and who meet other eligibility criteria. Rates of patient enrollment are affected by many factors, including the size of the patient population, the eligibility criteria for the clinical trial, the age and condition of the patients, the stage and severity of disease, the nature of the protocol, the proximity of patients to clinical sites and the availability of effective treatments for the relevant disease.

A product candidate can unexpectedly fail at any stage of preclinical and clinical development. The historical failure rate for product candidates is high due to scientific feasibility, safety, efficacy, changing standards of medical care and other variables. The results from preclinical testing or early clinical trials of a product candidate may not predict the results that will be obtained in later phase clinical trials of the product candidate. We, the FDA or other applicable regulatory authorities may suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects participating in such trials are being exposed to unacceptable health risks or adverse side effects. 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 Investigational New Drug applications (INDs) or comparable foreign applications or delays or failure in obtaining the necessary approvals from regulators 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 regarding the scope or design of our clinical trials;
- delays in enrolling research subjects in clinical trials;
- high drop-out rates of research subjects;

inadequate supply or quality of product candidate components or materials or other supplies necessary for the conduct of our clinical trials;

greater than anticipated clinical trial costs;

poor effectiveness of our product candidates during clinical trials;

unfavorable FDA or other regulatory agency inspection and review of a clinical trial site;

failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;

delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular; or

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

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

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

If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of preclinical studies or clinical trials or meet expected deadlines, our clinical development programs could be delayed and otherwise adversely affected. In all events, we are responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. The FDA requires clinical trials to be conducted in accordance with good clinical practices, including 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 and clinical development materials may become limited or interrupted or may not be of satisfactory quantity or quality.

We rely on third party supply and manufacturing partners to supply the materials and components for, and manufacture, our research and development, preclinical and clinical trial drug supplies. We do not own manufacturing facilities or supply sources for such components and materials. Our manufacturing requirements include lipid nanoparticle components and nucleic acid, each of which we procure from a single source supplier on a purchase order basis. In addition, we currently contract with only one drug product formulation manufacturer for the encapsulation of the oligonucleotide in a lipid particle. There can be no assurance that our supply of research and development, preclinical and clinical development 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 product formulation manufacturer could require significant effort and expertise because there may be a limited number of qualified replacements.

The manufacturing process for a product candidate is subject to FDA and foreign regulatory authority review. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as current Good Manufacturing Practices (cGMP). In the event that any of our suppliers or manufacturers fails to comply with such requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may 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 and guidelines. 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 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 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 arrangement with KHK, 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 not be able to maintain any new or existing collaboration if, for example, development or approval of a product candidate is delayed, sales of an approved product candidate do not meet expectations or the collaborator

terminates the collaboration. Any such collaboration, or other strategic transaction, may require us to incur non-recurring or other charges, increase our near- and long-term expenditures and pose significant integration or implementation challenges or disrupt our management or business. These transactions would entail numerous operational and financial risks, including exposure to unknown liabilities, disruption of our business and diversion of our management s time and attention in order to manage a collaboration or develop acquired products, product candidates or technologies, incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs, higher than expected collaboration, acquisition or integration costs, write-downs of assets or goodwill or impairment charges, increased amortization expenses, difficulty and cost in facilitating the collaboration or combining the operations and personnel of any acquired business, impairment of relationships with key suppliers, manufacturers or customers of any acquired business due to changes in management and ownership and the inability to retain key employees of any acquired business. Accordingly, although there can be no assurance that we will undertake or

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successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks and have a material adverse effect on our business, results of operations, financial condition and prospects. Conversely, any failure to enter any collaboration or other strategic transaction that would be beneficial to us could delay the development and potential commercialization of our product candidates and have a negative impact on the competitiveness of any product candidate that reaches market.

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

The development and commercialization of drugs is highly competitive. We compete with a variety of multinational pharmaceutical companies and specialized biotechnology companies, as well as technology being developed at universities and other research institutions. Our competitors have developed, are developing or will develop product candidates and processes competitive with our product candidates. Competitive therapeutic treatments include those that have already been approved and accepted by the medical community and any new treatments that enter the market. We 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 are aware of multiple companies that are working in the field of RNAi therapeutics, including major pharmaceutical companies such as Novartis International AG, Takeda Pharmaceutical Company Limited and biopharmaceutical companies such as Alnylam Pharmaceuticals, Inc. (Alnylam), which has recently closed the acquisition of Sirna Therapeutics, Inc. from Merck & Co., Inc., Tekmira Pharmaceuticals Corporation (Tekmira), Arrowhead Research Corporation (Arrowhead), Silence Therapeutics plc, RXi Pharmaceuticals Corporation, Quark Pharmaceuticals, Inc. and Marina Biotech, Inc. In particular, Arrowhead holds a non-exclusive license to the same patent rights of City of Hope (COH) and Integrated Data Technologies, Inc. (IDT) as we are licensed under our license agreement with COH. As a result, we cannot rely on those patent rights to prevent Arrowhead or third parties working with Arrowhead from developing, marketing and selling products that compete directly with our product candidates.

We also compete with companies working to develop antisense and other RNA-based drugs. Like RNAi therapeutics, antisense drugs target messenger RNA (mRNA) with the objective of suppressing the activity of specific genes. The development of antisense drugs is more advanced than that of RNAi therapeutics, and antisense technology may become the preferred technology for products that target mRNAs. Significant competition also exists from companies such as Tekmira 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.

If our lead product candidates are approved for the indications we are currently pursuing, they will compete with a range of therapeutic treatments that are either in development or currently marketed. For example, Nexavar, marketed by Amgen Inc. and Bayer AG, is currently in use for the treatment of hepatocellular carcinoma (HCC). Given the high unmet medical need and the commercial success of Nexavar, numerous targeted therapies for the treatment of HCC are under development. Targeted therapies represent the largest proportion of the HCC pipeline. There are also a number of pharmaceuticals and biologics that are marketed or in clinical development for the treatment of solid tumors. The most common treatments for solid tumors are various chemotherapeutic agents, radiation therapy and certain targeted therapies, including monoclonal antibodies such as Avastin, Erbitux, Herceptin and Vectibix. Small molecules, such as Nexavar, Sutent and Tarceva, are also indicated for the treatment of solid tumors. In addition, we believe that Kadmon Corporation, LLC is evaluating salirasib (KD032) in clinical trials for the treatment of KRAS-specific non-small cell lung cancer, pancreatic cancer and other solid tumors.

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 the safety and effectiveness of our products, the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. 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. Such 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, James B. Weissman, our chief business officer, and James E. Dentzer, our chief financial officer. The loss of one or more members of our management team or other key employees or advisors could delay our research and development programs and materially harm our business, financial condition, results of operations and prospects. The relationships that our key managers have cultivated within our industry make us particularly dependent upon their continued employment with us. We are dependent on the continued service of our technical personnel because of the highly technical nature of our product candidates and technologies and the specialized nature of the regulatory approval process. Because our management team and key employees are not obligated to provide us with continued service, they could terminate their employment with us at any time without penalty. We do not maintain key person life insurance policies on any of our management team members or key employees. Our future success will depend in large part on our continued ability to attract and retain other highly qualified scientific, technical and management personnel, as well as personnel with expertise in clinical testing, manufacturing, governmental regulation and commercialization. We face competition for personnel from other companies, universities, public and private research institutions, government entities and other organizations.

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

We have limited experience in drug development and have not begun clinical trials for any of our 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 or partners, suppliers and other organizations. Our ability to manage our operations and future growth will require us to continue to improve our operational, financial and management controls, reporting systems and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls.

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

We currently have no sales, marketing or distribution capabilities or experience. If any of our product candidates is approved, we will need to develop internal sales, marketing and distribution capabilities to commercialize such products, which would be expensive and time-consuming, or enter into collaborations with third parties to perform

these services. If we decide to market our products directly, we will need to commit

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

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

Even if we receive marketing and commercialization approval of a product candidate, we will be 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 has significant post-market authority, including the authority to require labeling changes based on new safety information and to require post-market studies or clinical trials to evaluate safety risks related to the use of a product or to require withdrawal of the product from the market. The FDA also has the authority to require a risk evaluation and mitigation strategies (REMS) plan after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug. The 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 letters, holds on clinical trials, refusal by the FDA to approve pending applications or supplements to approved applications, suspension or withdrawal of regulatory approval, product recalls and seizures, refusal to permit the import or export of products, operating restrictions, injunction, civil penalties and criminal prosecution.

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

In some countries, particularly member states of the European Union, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we or our collaborators may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our RNAi therapeutic candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further

pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of any product candidate approved for marketing is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, financial condition, results of operations or prospects could be adversely affected.

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

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, provide accurate information to 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 and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions 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 or regulations. 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 or other sanctions.

Our internal computer systems, or those of our CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite the implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such events could cause interruptions of our operations. For instance, the loss of preclinical data or data from any future clinical trial involving our product candidates could result in delays in our development and regulatory filing efforts and significantly increase our costs. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the development of our product candidates could be delayed.

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

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

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

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

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

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

We have incurred substantial losses during our history, do not expect to become profitable for the foreseeable future and may never achieve profitability. To the extent that we continue to generate taxable losses,

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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 closed on February 4, 2014, and our net operating losses are subject to such limitation. As of December 31, 2013, we had U.S. federal and Massachusetts net operating loss carryforwards of $65.1 million and $64.6 million, respectively. Any limit on these loss carryforwards if we have or do experience an ownership change could have an adverse effect on our business, financial position, results of operations and prospects.

The investment of our cash, cash equivalents and fixed income marketable securities is subject to risks which may cause losses and affect the liquidity of these investments.

As of December 31, 2013, we had $46.6 million in cash and cash equivalents and fixed income marketable securities. In addition, we received approximately $92.9 million of net proceeds, after deducting the underwriting commissions and discounts and the offering expenses payable by us, from the initial public offering of 6,900,000 shares of our common stock closed on February 4, 2014. We historically have invested substantially all of our available cash and cash equivalents in corporate bonds, commercial paper, securities issued by the U.S. government, certificates of deposit and money market funds meeting the criteria of our investment policy, which is focused on the preservation of our capital. These investments are subject to general credit, liquidity, market and interest rate risks, including the impact of U.S. sub-prime mortgage defaults that have affected various sectors of the financial markets and caused credit and liquidity issues. We may realize losses in the fair value of these investments or a complete loss of these investments, which would have a negative effect on our condensed 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 relevant accounting authorities, including the 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 financial statements, including those contained in this Annual Report on Form 10-K.

Risks Related to Intellectual Property

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

Our success depends in part on our ability to obtain and maintain patents and other forms of intellectual property rights, including in-licenses of intellectual property rights of others, for our product candidates, methods used to manufacture our product candidates and methods for treating patients using our product candidates, as well as our ability to preserve our trade secrets, to prevent third parties from infringing upon our proprietary rights and to operate

without infringing upon the proprietary rights of others. As of March 1, 2014, our patent

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estate, including the patents and patent applications that we have licensed from COH included approximately 16 issued patents and approximately 67 pending patent applications for research and development of our DsiRNA molecules and delivery technologies. We may not be able to apply for patents on certain aspects of our product candidates or delivery technologies in a timely fashion or at all. Our existing issued and granted patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing products and technology. There is no guarantee that any of our pending patent applications will result in issued or granted patents, that any of our issued or granted patents will not later be found to be invalid or unenforceable or that any issued or granted patents will include claims that are sufficiently broad to cover our product candidates or delivery technologies or to provide meaningful protection from our competitors. Moreover, the patent position of biotechnology and pharmaceutical companies can be highly uncertain because it involves complex legal and factual questions. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our current and future proprietary technology and product candidates are covered by valid and enforceable patents or are effectively maintained as trade secrets. If third parties disclose or misappropriate our proprietary rights, it may materially and adversely impact our position in the market.

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

In addition, there are numerous recent changes to the patent laws and proposed changes to the rules of the USPTO which may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, the America Invents Act (AIA) enacted within the last several years involves significant changes in patent legislation. The 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 recent decision by the 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 which contain modifications that we believe are not found in nature. However, this decision has yet to be clearly interpreted by courts and by the USPTO. We cannot assure you that the interpretations of this decision or subsequent rulings will not adversely impact our patents or patent applications. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Once granted, patents may remain open to opposition, interference, re-examination, post-grant review, inter partes review, nullification or derivation action in court or before patent offices or similar proceedings for a given period 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. In addition, there can be no assurance that:

- Others will not or may not 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.

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We or our licensors, collaborators or any future collaborators are the first to make the inventions covered by each of our issued patents and pending patent applications that we own or license.

We or our licensors, collaborators or any future collaborators are the first to file patent applications covering certain aspects of our inventions.

Others will not independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.

A third party may not challenge our patents and, if challenged, a court may not hold that our patents are valid, enforceable and infringed.

Any issued patents that we own or have licensed will provide us with any competitive advantages, or will not be challenged by third parties.

We may develop additional proprietary technologies that are patentable.

The patents of others will not have an adverse effect on our business.

Our competitors do not conduct research and development activities in countries where we do 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.

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

We do, and will continue to, rely on intellectual property rights licensed from third parties to protect our technology. We are a party to a number of licenses that give us rights to third-party intellectual property that is necessary or useful for our business. In particular, we have a license from COH (on behalf of itself and IDT) to certain patent rights, which provide platform intellectual property for research and development of our DsiRNA molecules. Pursuant to this agreement, we have a worldwide license from COH (subject to the pre-existing non-exclusive license) for the exploitation of key intellectual property rights in this respect, and COH and IDT retain ownership of the patents and patent applications to which we are licensed under the agreement. See the description set forth in Item 1 Business-Strategic Partnerships and Collaborations City of Hope license agreement. We also intend to license additional third-party intellectual property in the future. Our success will depend in part on the ability of our licensors to obtain, maintain and enforce patent protection for our licensed intellectual property, in particular, those patents to which we have secured exclusive rights. Our licensors may not successfully prosecute the patent applications licensed to us. Even if patents issue or are granted, our licensors may fail to maintain these patents, may determine not to pursue litigation against other companies that are infringing these patents, or may pursue litigation less aggressively than we would. Further, we may not obtain exclusive rights, which would allow for third parties to develop competing products. Without protection for, or exclusive right to, the intellectual property we license, other companies might be

able to offer substantially identical products for sale, which could adversely affect our competitive business position and harm our business prospects. In addition, we sublicense our rights under our third-party licenses to KHK and may sublicense such rights to current or future collaborators or any future strategic partners. Any impairment of these sublicensed rights could result in reduced revenue under our collaboration agreement with KHK or result in termination of an agreement by one or more of our collaborators or any future strategic partners.

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

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

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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 Research Corporation (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 DsiRNA 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 adversely affect our revenue, financial condition and results of operations.

Other companies or organizations may challenge our or our licensors patent rights or may assert patent rights that prevent us from developing and commercializing our products.

RNAi therapeutics are relatively new scientific fields, the commercial exploitation of which has resulted in many different patents and patent applications from organizations and individuals seeking to obtain patent protection in the field. We have obtained grants and issuances of RNAi, RNAi therapeutic and DsiRNA patents and have licensed many of these patents from third parties on an exclusive or non-exclusive basis. The issued patents and pending patent applications in the U.S. and in key markets around the world that we own or license claim many different methods, compositions and processes relating to the discovery, development, manufacture and commercialization of RNAi therapeutics and DsiRNA therapeutics. Specifically, we own and have licensed a portfolio of patents, patent applications and other intellectual property covering: (1) certain aspects of the structure and uses of DsiRNAs, including their manufacture and use as therapeutics, and DsiRNA-related mechanisms, (2) chemical modifications to DsiRNAs that improve their suitability for therapeutic uses, (3) DsiRNAs directed to specific gene sequences and drug targets as treatments for particular diseases and (4) delivery technologies, such as in the field of lipid chemistry, lipid nanoparticles and lipid nanoparticle formulation.

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, reexamination and opposition 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 DsiRNA 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 DsiRNA therapeutic candidates. There are also many issued patents that claim targeting

genes or portions of genes that may be relevant for DsiRNA 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 not be able to market products or perform research and development or other activities covered by these patents.

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We may not be able to protect our intellectual property rights throughout the world.

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

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

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

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

We or our licensors, collaborators or any future strategic partners may be subject to third-party claims for infringement or misappropriation of patent or other proprietary rights. We are generally obligated under our license or collaboration agreements to indemnify and hold harmless our licensors or collaborator for damages arising from intellectual property infringement by us. If we or our licensors, collaborators or any future strategic partners are found

to infringe a third party patent or other intellectual property rights, we could be required to pay damages, potentially including treble damages, if we are found to have willfully infringed. In addition, we or our licensors, collaborators or any future strategic partners may choose to seek, or be required to seek, a license from a third party, which may not be available on acceptable terms, if at all. Even if a license can be obtained on

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acceptable terms, the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. If we fail to obtain a required license, we or our collaborator, or any future collaborator, may be unable to effectively market product candidates based on our technology, which could limit our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. In addition, we may find it necessary to pursue claims or initiate lawsuits to protect or enforce our patent or other intellectual property rights. The cost to us in defending or initiating any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in our favor, could be substantial, and litigation would divert our management s attention. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations.

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

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 or licenses could be costly or not available on commercially reasonable terms.

Because the RNAi intellectual property landscape is still evolving, it is difficult to conclusively assess our freedom to operate without infringing on third party rights. There are numerous companies that have pending patent applications and issued patents broadly directed to RNAi generally and to RNAi delivery technologies. Our competitive position may suffer if patents issued to third parties or other third party intellectual property rights cover our products or elements thereof, or our manufacture or uses relevant to our development plans. In such cases, we may not be in a position to develop or commercialize products or product candidates unless we successfully pursue litigation to nullify or invalidate the third party intellectual property right concerned, or enter into a license agreement with the intellectual property right holder, if available on commercially reasonable terms. For instance, we received a letter from Alnylam in March 2010, claiming that we require access to certain patent and patent applications owned or controlled by Alnylam and demanding that we cease and desist from alleged infringing activities unless and until we obtain a license from Alnylam for the necessary intellectual property. We have disputed Alnylam s claims and engaged in several discussions with Alnylam. We have not received any further correspondence from Alnylam since 2010 regarding this claim. However, there can be no assurance that Alnylam will not continue to pursue this or other claims against us. We are aware of issued patents, and there may be others of which we are not aware, held by third parties that, if found to be valid and enforceable, could be alleged to be infringed by our DsiRNA molecules. We are also aware of pending patent applications, and there may be others of which we are not aware, that if they result in issued

patents, could be alleged to be infringed by our DsiRNA molecules. If such an infringement claim should be brought and be successful, we may be required to pay substantial damages, be forced to abandon our product candidates or seek a license from any patent holders. No assurances can be given that a license will be available on commercially reasonable terms, if at all.

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For example, we are aware of a European patent, granted in 2006, and assigned to Alnylam (EP 1 352 061 B1) (EP 061 patent), that broadly covers various RNAi constructs, including potentially our DsiRNA molecules. The EP 061 patent has been validated and is currently in force in Austria, Germany, Ireland, Liechtenstein, Switzerland, and the United Kingdom. It has not yet been validated in any other European countries. Another third party, Sirna Therapeutics, Inc., formerly a wholly-owned subsidiary of Merck & Co., Inc., filed an opposition seeking to revoke the EP 061 patent as invalid. In August 2009, the Opposition Division of the European Patent Office (EPO) rejected the opposition and upheld all of the claims of the EP 061 patent as originally granted. That decision is currently on appeal by Sirna Therapeutics. We are currently not a party to the opposition. In March 2014, Alnylam announced that it has completed the acquisition of Sirna Therapeutics from Merck & Co., Inc., and the appeal may therefore be terminated, in which case we would not be able to join or continue the opposition in the EPO, though we could seek to challenge this patent in the individual European countries where it has been validated. If the EP 061 patent remains in force in each validated European country, we could be prevented from commercializing our DsiRNA products in each of those countries and we could be sued for patent infringement in such countries. We are aware that others are pursuing patent applications directed to similar subject matter in the U.S. and other jurisdictions and reinstatement of a revoked European patent broadly covering various RNA constructs. If any one of these applications were ultimately to issue as patents or the revoked patent were reinstated with claims that cover our DsiRNA molecules, their methods of use or methods of delivery, we could be sued for patent infringement in each of those countries as well. If we were unsuccessful in defending ourselves in any of these actions, we may be required to pay substantial damages, be forced to abandon our product candidates or seek a license from any patent holders, in each case, in such countries. We believe that the expected expiration date of the EP 061 patent and any foreign counterparts that might issue is early 2022.

It is also possible that we have failed to identify relevant third party patents or applications. For example, U.S. applications filed before November 29, 2000 and certain U.S. applications filed after that date that will not be filed outside the U.S. remain confidential until patents issue. Patent applications in the U.S. and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our products or platform technology could have been filed by others without our knowledge. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our platform technologies, our products or the use of our products. Third party intellectual property right holders may also actively bring infringement claims against us. We cannot guarantee that we will be able to successfully settle or otherwise resolve such 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, if possible, 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.

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

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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 may be 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 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. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of 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. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

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

Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our

markets of interest. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

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Risks Related to Government Regulation

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

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

We have very limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA. The time required to obtain FDA and other 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 FDA policy during the period of product development, clinical trials and FDA regulatory review. It is impossible to predict whether legislative changes will be enacted, or whether FDA or foreign regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be.

Because the drugs we are developing may represent a new class of drug, the FDA and its foreign counterparts have not yet established any definitive policies, practices or guidelines in relation to these drugs. While we believe the product candidates that we are currently developing are regulated as new drugs under the Federal Food, Drug, and Cosmetic Act, the FDA could decide to 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 of any regulatory filings that we may submit. Moreover, the FDA 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. Furthermore, in recent years, there has been increased public and political pressure on the FDA with respect to the approval process for new drugs, and the FDA s standards, especially regarding drug safety, appear to have become more stringent.

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. In addition, the FDA has the authority to require a Risk Evaluation and Mitigation Strategy (REMS) plan as part of an NDA or biologics license application (BLA) or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug or biologic, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry. These limitations and

restrictions may limit the size of the market for the product and affect reimbursement by third-party payors.

We are also subject to numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process varies among countries and may include all of the risks associated with FDA approval

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described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval. Approval by the FDA does not ensure approval by regulatory authorities outside the U.S. and vice versa.

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

We and our collaborators are subject to federal, state, and foreign healthcare laws and regulations pertaining to fraud and abuse and patients rights. These laws and regulations include:

- the U.S. federal healthcare program anti-kickback law, which prohibits, among other things, persons from soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual for a healthcare item or service, or the purchasing or ordering of an item or service, for which payment may be made under a federal healthcare program such as Medicare or Medicaid;

- the U.S. federal false claims law, which prohibits, among other things, individuals or entities from knowingly presenting or causing to be presented, claims for payment by government funded programs such as Medicare or Medicaid that are false or fraudulent, and which may apply to us by virtue of statements and representations made to customers or third parties;

- the U.S. federal Health Insurance Portability and Accountability Act (HIPAA) and Health Information Technology for Economic and Clinical Health (HITECH) Act, which prohibit executing a scheme to defraud healthcare programs, impose requirements relating to the privacy, security, and transmission of individually identifiable health information, and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information;

- the federal Open Payments regulations under the National Physician Payment Transparency Program have been issued under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, and will require that manufacturers of pharmaceutical and biological drugs covered by Medicare, Medicaid, and Children s Health Insurance Programs report all consulting fees, travel reimbursements, research grants, and other payments or gifts with values over $10 made to physicians and teaching hospitals; and

- state laws comparable to each of the above federal laws, such as, for example, anti-kickback and false claims laws applicable to commercial insurers and other non-federal payors, requirements for mandatory corporate regulatory compliance programs, and laws relating to patient data privacy and security.

If our operations are found to be in violation of any such requirements, we may be subject to penalties, including civil or criminal penalties, monetary damages, the curtailment or restructuring of our operations, loss of eligibility to obtain approvals from the FDA, or exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, any of which could adversely 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 our collaborators, manufacturers or service providers fail to comply with applicable federal, state or foreign laws or regulations, we could be subject to enforcement actions, which could affect our ability to develop, market and sell our products successfully and could harm our reputation and lead to reduced acceptance of our products by the market. These enforcement actions include, among others:

adverse regulatory inspection findings;

warning letters;

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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;

suspension or withdrawal of product approvals;

product seizures;

injunctions; and

civil and criminal penalties and fines.

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

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

Our ability to commercialize any products successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Even if we succeed in bringing one or more products to the market, these products may not be considered cost-effective, and the amount reimbursed for any products may be insufficient to allow us to sell our products on a competitive basis. Because our programs are in the early stages of development, we are unable at this time to determine their cost effectiveness or the likely level or method of reimbursement.

Increasingly, the third-party payors who reimburse patients or healthcare providers, such as government and private insurance plans, are requiring that drug companies provide them with predetermined discounts from list prices, and are seeking to reduce the prices charged or the amounts reimbursed 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/some drugs we develop may need to be administered under the supervision of a physician on an outpatient basis. Under currently applicable U.S. law, certain drugs that are not usually self-administered (including injectable drugs) may be eligible for coverage under the Medicare Part B program if:

they are incident to a physician s services;

they are reasonable and necessary for the diagnosis or treatment of the illness or injury for which they are administered according to accepted standards of medical practice; and

they have been approved by the FDA and meet other requirements of the statute.

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There may be significant delays in obtaining coverage for newly-approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA. Moreover, eligibility for coverage does not imply that any drug will be reimbursed in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim payments for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement may be based on payments allowed for lower-cost drugs that are already reimbursed, may be incorporated into existing payments for other services and may reflect budgetary constraints or imperfections in Medicare data. Net 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. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for new drugs that we develop and for which we obtain regulatory approval could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our financial condition.

We believe that the efforts of governments and third-party payors to contain or reduce the cost of healthcare and legislative and regulatory proposals to broaden the availability of healthcare will continue to affect the business and financial condition of pharmaceutical and biopharmaceutical companies. A number of legislative and regulatory changes in the healthcare system in the U.S. and other major healthcare markets have been proposed in recent years, and such efforts have expanded substantially in recent years. These developments have included prescription drug benefit legislation that was enacted and took effect in January 2006, healthcare reform legislation enacted by certain states, and major healthcare reform legislation that was passed by Congress and enacted into law in the U.S. in 2010. These developments could, directly or indirectly, affect our ability to sell our products, if approved, at a favorable price.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act (ACA), a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending and enhance remedies against fraud and abuse. The ACA also contains provisions that will affect companies in the pharmaceutical industry and other healthcare related industries by imposing additional costs and changes to business practices. Provisions affecting pharmaceutical companies include the following.

Mandatory rebates for drugs sold into the Medicaid program have been increased, and the rebate requirement has been extended to drugs used in risk-based Medicaid managed care plans.

The 340B Drug Pricing Program under the Public Health Services Act has been extended to require mandatory discounts for drug products sold to certain critical access hospitals, cancer hospitals and other covered entities.

Pharmaceutical companies are required to offer discounts on brand-name drugs to patients who fall within the Medicare Part D coverage gap, commonly referred to as the Donut Hole.

Pharmaceutical companies are required to pay an annual non-tax deductible fee to the federal government based on each company s market share of prior year total sales of branded products to certain federal healthcare programs, such as Medicare, Medicaid, Department of Veterans Affairs and Department of Defense. Since we expect our branded pharmaceutical sales to constitute a small portion of the total federal health program pharmaceutical market, we do not expect this annual assessment to have a material impact on our financial condition.

For product candidates classified as biologics, approval of an application 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 will be easier for biosimilar manufacturers to enter the market, which is likely to reduce the pricing for such products and could affect our profitability.

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The full effects of the U.S. healthcare reform legislation cannot be known until the new law is fully implemented through regulations or guidance issued by the Centers for Medicare & Medicaid Services and other federal and state healthcare agencies. The financial impact of the U.S. healthcare reform legislation over the next few years will depend on a number of factors, including but not limited to, the policies reflected in implementing regulations and guidance and changes in sales volumes for products affected by the new system of rebates, discounts and fees. The new legislation may also have a positive impact on our future net sales, if any, by increasing the aggregate number of persons with healthcare coverage in the U.S., but such increases are unlikely to be realized until approximately 2014 at the earliest.

Moreover, we cannot predict what healthcare reform initiatives may be adopted in the future. Further federal and state legislative and regulatory developments are likely, and we expect ongoing initiatives in the U.S. to increase pressure on drug pricing. 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.

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

U.S. federal government agencies currently face potentially significant spending reductions. Under the Budget Control Act of 2011, the failure of Congress to enact deficit reduction measures of at least $1.2 trillion for the years 2013 through 2021 triggered automatic cuts to most federal programs. These cuts would include aggregate reductions to Medicare payments to providers of up to two percent per fiscal year, starting in 2013. Under the American Taxpayer Relief Act of 2012, which was enacted on January 1, 2013, the imposition of these automatic cuts was delayed until March 1, 2013. Certain of these automatic cuts have been implemented. The full impact on our business of these automatic cuts is uncertain. 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 receives marketing approval and we or others later identify undesirable side effects caused by the product candidate, our ability to market and derive revenue from the product candidates could be compromised.

In the event that any of our product candidates receive regulatory approval and we or others identify undesirable side effects 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 be required to recall the product or change the way the product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof;

we may be subject to fines, injunctions or the imposition of civil or criminal penalties;

regulatory authorities may require the addition of labeling statements, such as a black box warning or a contraindication;

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;

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the product may become less competitive; and

our reputation may suffer.

Risks Related to Our Common Stock

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

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

Our stock price is volatile. From January 30, 2014, the first day of trading of our common stock, through March 26, 2014, our stock had high and low closing sale prices in the range of $46.00 and $30.36 per share. The market price for our common stock may be influenced by many factors, including, but not limited to, the other risks described in this section of this Annual Report on Form 10-K titled Risk Factors and the following:

the success of competitive products or technologies;

results of preclinical and clinical studies of our product candidates, or those of our competitors, our existing collaborator or any future collaborators;

regulatory or legal developments in the U.S. and other countries, especially changes in laws or regulations applicable to our products;

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

actions taken by regulatory agencies with respect to our 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;

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the success of our efforts to acquire or in-license additional technologies, products or product candidates;

developments concerning our collaborations, including but not limited to those with our sources of manufacturing supply and our commercialization partners;

announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;

developments or disputes concerning patents or other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our products;

our ability or inability to raise additional capital and the terms on which we raise it;

the recruitment or departure of key personnel;

changes in the structure of healthcare payment systems;

market conditions in the pharmaceutical and biotechnology sectors;

actual or anticipated changes in earnings estimates or changes in stock market analyst recommendations regarding our common stock, other comparable companies or our industry generally;

our failure or the failure of our competitors to meet analysts projections or guidance that we or our competitors may give to the market;

fluctuations in the valuation of companies perceived by investors to be comparable to us;

announcement and expectation of additional financing efforts;

speculation in the press or investment community;

trading volume of our common stock;

sales of our common stock by us or our stockholders;

the absence of lock-up agreements in connection with the initial public offering of our common stock with the holders of substantially all of our outstanding shares;

the concentrated ownership of our common stock;

changes in accounting principles;

terrorist acts, acts of war or periods of widespread civil unrest;

natural disasters and other calamities; and

general economic, industry and market conditions.

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

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

We may choose to raise additional capital in the future, depending on market conditions, strategic considerations and operational requirements. To the extent that additional capital is raised through the issuance of shares or other securities convertible into shares, our stockholders will be diluted. Future issuances of our common stock or other equity securities, or the perception that such sales may occur, could adversely affect the trading price of our common stock and impair our ability to raise capital through future offerings of shares or equity securities. No prediction can be made as to 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.

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Substantially all of our outstanding shares are not subject to lock-up agreements in connection with the initial public offering of our common stock. The sale of a significant number of our shares may cause the market price of our common stock to drop significantly.

Our executive officers have entered into lock-up agreements with the underwriters for the initial public offering of our common stock under which they have agreed, subject to specific exceptions, not to sell shares of our common stock or securities exchangeable or exercisable therefor owned by them for a period of 180 days after the date of the final prospectus for the offering. These restrictions are due to expire on July 28, 2014. However, the holders of substantially all of our shares of common stock and securities convertible or exercisable into shares of our common stock outstanding at the time of the offering have not entered into any lock-up agreements in connection with the initial public offering. As a result, a substantial number of shares of our common stock, including shares of common stock issuable upon exercise of outstanding warrants, are available for sale in the public market after the completion of the initial public offering on February 4, 2014. The sale of a significant number of shares of our comment stock in the public market or the perception that such sale may occur could significantly reduce the market price of our common stock.

In addition, we filed a registration statement on Form S-8 on February 6, 2014 registering the issuance of a total of 4,369,672 shares of common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. The shares registered under such registration statement will be available for sale in the public market subject to vesting arrangements and exercise of options, the lock-up agreements of our executive officers as described above, our insider trading policy and volume limitations applicable to affiliates under Rule 144.

Moreover, the holders of a substantial number of shares of our common stock, including shares of common stock issuable upon exercise of outstanding warrants, have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. If such holders, by exercising their registration rights, cause a large number of securities to be registered and sold into the public market, these sales could have an adverse effect on the market price for our common stock.

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

Our executive officers are parties to employment agreements providing, in the event of a termination of employment in connection with a change of control of us, for aggregate cash payments of up to approximately $1.5 million 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 harm 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.

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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.

Immediately after the closing of the initial public offering of our common stock on February 4, 2014, our executive officers and directors, together with holders of five percent or more of our outstanding common stock and their respective affiliates, beneficially own, in the aggregate, approximately 70.5 percent of our outstanding common stock based upon information supplied to us by our executive officers, directors and Schedules 13D or 13G filed with the SEC. As a result, these stockholders, if acting together, will continue to have significant influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets and any other significant corporate transaction. The interests of these stockholders may not be the same as or may even conflict with the interests of our other stockholders. For example, these stockholders could delay or prevent a change of control of our company, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might affect the prevailing market price of our common stock. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors perception that conflicts of interest may exist or arise.

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

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

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

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

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

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the NASDAQ and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may 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 SEC s rules that implement Section 404 of the Sarbanes-Oxley Act (Section 404), and are therefore not required to make a formal assessment of the effectiveness of our internal control over financial reporting for that purpose. Pursuant to Section 404, we will be required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 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 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. In addition, our loan and security agreement with Hercules Technology II, L.P. (Hercules) currently prohibits us from paying dividends on our equity securities, and any future debt agreements may likewise preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

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

Our stock price 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 may be, holders of that stock have occasionally

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

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

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

Item 1B. ***Unresolved Staff Comments***

None.

Item 2. ***Properties***

Our corporate headquarters are located in Watertown, Massachusetts, where we lease 15,174 square feet of office and laboratory space. The lease term for our office and laboratory space in Watertown, Massachusetts, commenced in October 2008 for a lease term of five years. On July 3, 2013, the lease agreement was amended to extend the term for an additional three years, which expires in November 2016, with an option to extend the lease for an additional term of two 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.

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

Not applicable.

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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 has been publicly traded on The NASDAQ Global Select Market under the symbol DRNA since January 30, 2014. Prior to that time, there was no public market for our common stock. As a result, we have not set forth information with respect to the high and low prices of our common stock for any full fiscal quarter within the two most recent fiscal years.

On March 26, 2014, the closing sale price for our common stock as reported on The NASDAQ Global Select Market was $32.20 per share.

Holders of Record

As of March 26, 2014, there were approximately 36 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 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.

Securities Authorized for Issuance Under Equity Compensation Plans

Information regarding our equity compensation plans as of December 31, 2013 is disclosed in Item 12 Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters of this Annual Report on Form 10-K and is incorporated herein by reference from our proxy statement for our 2014 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission (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.

Recent Sales of Unregistered Securities

The following sets forth information regarding all securities sold or granted by us during the fiscal year ended December 31, 2013, which were not registered under the Securities Act of 1933, as amended (Securities Act), and the consideration, if any, received by us for such securities.

We effected a reverse stock split upon the filing of an amended and restated certificate of incorporation with the Secretary of State of the State of Delaware on July 25, 2013, pursuant to which (a) each 250 shares of our common stock outstanding immediate prior to the effectiveness of the reverse stock split were combined and converted into one

share of our common stock outstanding immediately thereafter and (b) each 25 shares of our Series A and Series B preferred stock outstanding immediately prior to the effectiveness of the reverse stock split were combined and converted into one share of our Series A and Series B preferred stock outstanding immediately thereafter. The numbers of securities and the purchase price or exercise price per share set forth below have been adjusted for the effect of the reverse stock split described above.

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Immediately prior to the consummation of the initial public offering of our common stock on February 4, 2014, all of then-outstanding shares of our Series A, Series B and Series C preferred stock were converted into shares of our common stock on a one-for-one basis and all of the then-outstanding warrants to purchase our Series A, Series B and Series C preferred stock became exercisable to purchase shares of our common stock.

Issuance of Series C preferred stock

(1) On July 30, 2013, we issued and sold to eighteen accredited investors an aggregate of 8,571,417 shares of our Series C preferred stock at a purchase price of $7.00 per share for an aggregate consideration of $57,000,237 in cash and $2,999,700 of aggregate principal amount of convertible promissory notes, issued by us on June 26, 2013 to seven of the eighteen investors (2013 bridge note financing), converted into shares of Series C preferred stock. Immediately prior to the consummation of our initial public offering, each share of Series C preferred stock converted into one share of our common stock.

Issuance of warrants to purchase Series C preferred stock

(2) On June 26, 2013, we issued seven warrants to purchase an aggregate of 85,703 shares of our Series C preferred stock to seven investors for an aggregate warrant purchase price of $300.00 in connection with our 2013 bridge note financing. Each warrant has an exercise price of $7.00 per share of our Series C preferred stock. These warrants became exercisable for 85,703 shares of our common stock at an exercise price of $7.00 per share of our common stock immediately prior to the consummation of our initial public offering.

Grants of stock options and issuances of common stock

(3) From January 1, 2013 through December 31, 2013, we granted stock options to purchase an aggregate of 1,607,000 shares of our common stock with an exercise price of $3.42 per share to our employees, directors and consultants pursuant to our 2007 employee, director and consultant stock plan, as amended (the 2007 Plan), and our 2010 employee, director and consultant equity incentive plan, as amended (the 2010 Plan). From January 1, 2013 through December 31, 2013, we issued an aggregate of 10,358 shares of our common stock upon exercise of stock options granted pursuant to our 2007 Plan and 2010 Plan for aggregate cash consideration of $45,904.86

We deemed the offers, sales and issuances of the securities described in paragraphs (1) and (2) above to be exempt from registration under the Securities Act, in reliance on Section 4(2) of the Securities Act, including Regulation D and Rule 506 promulgated thereunder, relative to transactions by an issuer not involving a public offering. All purchasers of securities in transactions exempt from registration pursuant to Regulation D represented to us that they were accredited investors and were acquiring the shares for investment purposes only and not with a view to, or for sale in connection with, any distribution thereof and that they could bear the risks of the investment and could hold the securities for an indefinite period of time. The purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration statement or an available exemption from such registration.

We deemed the grants of stock options and issuances of common stock described in paragraph (3) above, except to the extent described above as exempt pursuant to Section 4(2) of the Securities Act, to be exempt from registration under the Securities Act in reliance on Rule 701 of the Securities Act as offers and sales of securities under compensatory benefit plans and contracts relating to compensation in compliance with Rule 701. Each of the recipients of securities in any transaction exempt from registration either received or had adequate access, through employment, business or other relationships, to information about us.

All of the foregoing securities are deemed restricted securities for purposes of the Securities Act. The certificates representing the securities issued in the transactions described above included appropriate legends setting forth that the securities had not been offered or sold pursuant to a registration statement and describing the applicable restrictions on transfer of the securities. There were no underwriters employed in connection with any of the transactions set forth above.

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Use of Proceeds from Initial Public Offering of Common Stock

On February 4, 2014, we completed the initial public offering of our common stock and sold and issued a total of 6,900,000 shares of our common stock, including 900,000 shares sold pursuant to the exercise in full by the underwriters of the option to purchase additional shares, at a public offering price of $15.00 per share for aggregate gross proceeds of $103.5 million before deducting underwriting commissions and discounts and offering expenses payable by us.

Jefferies LLC, Leerink Partners LLC, and Stifel, Nicolaus & Company, Incorporated acted as joint book-running managers for our initial public offering. Robert W. Baird & Co. Incorporated acted as co-lead manager for our initial public offering. We received net proceeds of approximately $92.9 million in our initial public offering after deducting underwriting commissions and discounts of $7,245,000 and offering expenses of $3.4 million. None of the offering expenses were paid to our directors, officers or persons owning ten percent or more of any class of our equity securities, or to any of their associates or our affiliates.

The shares of common stock were registered under the Securities Act on a registration statement on Form S-1 (File No. 333-193150). The SEC declared the registration statement effective on January 29, 2014. Shares of our common stock began trading on The NASDAQ Global Select Market on January 30, 2014. On February 4, 2014, following the sale of 6,900,000 shares of our common stock, our initial public offering ended.

Because the closing of our initial public offering occurred on February 4, 2014, as of December 31, 2013, we had not yet received the net proceeds from the sale of shares of common stock in our initial public offering and therefore had used none of the proceeds by December 31, 2013. There has been no material change in the planned use of proceeds from our initial public offering as described in the final prospectus dated as of January 29, 2014 for the initial public offering and filed with the SEC pursuant to Rule 424(b) under the Securities Act on January 30, 2014.

Purchases of Equity Securities by the Issuer and Affiliated Parties

None.

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

The selected consolidated financial data included within the tables below should be read in conjunction with our consolidated financial statements and related notes and the *Management s Discussion and Analysis of Financial Condition and Results of Operations* section of this Annual Report on Form 10-K.

SELECTED CONSOLIDATED FINANCIAL DATA

(in thousands, except share and per share data)

	YEARS ENDED DECEMBER 31,		
	2011	**2012**	**2013**
Results of operations			
Revenue	$ 7,908	$ 7,015	$
Operating expenses:			
Research and development	10,705	11,565	11,558
General and administrative	4,816	4,700	5,820
Total operating expenses	15,521	16,265	17,378
Loss from operations	(7,613)	(9,250)	(17,378)
Other income (expense):			
Preferred stock warrant remeasurement	51	469	126
Interest income	3	2	4
Loss on extinguishment of debt			(318)
Interest expense	(997)	(1,342)	(952)
Total other income (expense)	(943)	(871)	(1,140)
Net loss	$ (8,556)	$ (10,121)	$ (18,518)
Less: Accretion and dividends on redeemable convertible preferred stock	4,099	4,097	2,388
Net loss attributable to common stockholders	$ (12,655)	$ (14,218)	$ (20,906)
Net loss per share attributable to common stockholders basic and diluted	$ (492.76)	$ (516.00)	$ (709.57)
Weighted average shares outstanding basic and diluted	25,682	27,554	29,463
Financial condition			
Cash and cash equivalents	$ 22,490	$ 3,670	$ 46,595
Total assets	$ 24,637	$ 10,191	$ 49,794
Long-term debt net of current portion	$ 8,735	$ 4,660	$ 260
Total stockholders deficit	$ (50,633)	$ (64,719)	$ (68,919)

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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

We are a biopharmaceutical company focused on the discovery and development of innovative treatments for rare inherited diseases involving the liver and for cancers that are genetically defined. We are using our RNA interference (RNAi) technology platform to build a broad pipeline in these therapeutic areas. In both rare diseases and oncology, we are pursuing targets that have historically been difficult to inhibit using conventional approaches, but where we believe connections between targets and diseases are well understood and documented. We aim to discover, develop and commercialize these novel therapeutics either on our own or in collaboration with pharmaceutical partners. In indications such as rare diseases in which a small sales force will suffice, we seek to retain substantially all commercial rights in key markets. In oncology and other more prevalent disease areas, we may partner our products while seeking to retain significant portions of the commercial rights in North America.

In the rare disease field, we are developing a proprietary treatment, DCR-PH1, for the rare and serious inherited disorder Primary Hyperoxaluria 1 (PH1). We seek to begin clinical trials of DCR-PH1 in 2015. We also have discovery and early development programs against a series of additional disease targets in the liver. In oncology, we are currently directing our development efforts towards our proprietary product candidate DCR-M1711 for the treatment of MYC-related cancers, including hepatocellular carcinoma (HCC), which we believe represents 85 to 90 percent of primary liver cancer. We submitted an Investigational New Drug application for DCR-M1711 for the treatment of HCC to the U.S. Food and Drug Administration in the first quarter of 2014 and have received from the FDA a non-objection letter to initiate the Phase 1 development. We intend to begin clinical trials of DCR-M1711 in the first half of 2014.

As part of our collaboration with Kyowa Hakko Kirin Co., Ltd. (KHK), a global pharmaceutical company, we are developing a product candidate that targets the oncogene KRAS, which is frequently mutated in numerous major cancers, including non-small cell lung cancer, colorectal cancer, and pancreatic cancer. KHK is responsible for global development of the KRAS program, including all development expenses. For the KRAS product candidate, we retain an option to co-promote in the U.S. for an equal share of the profits from U.S. net sales. We are also developing a product candidate targeting another oncogene in collaboration with KHK. For each product candidate in our collaboration with KHK, we have the potential to receive clinical, regulatory and commercialization milestone payments of up to $110.0 million and royalties on net sales of each such product candidate. We expect that our strategy to partner the development of product candidates will help us fund the costs of clinical development and enable us to diversify risk across a number of programs.

Since our inception in October 2006, we have devoted substantial resources to the research and development of DsiRNA molecules and drug delivery technologies and the protection and enhancement of our intellectual property estate. We have no products approved for sale and all of our revenue to date has been collaboration revenue or government grant revenue. To date, we have funded our operations primarily through the recent initial public offering of our common stock, previous private placements of preferred stock and convertible debt securities, from research funding, license fees, option exercise fees and preclinical payments under our research collaboration and license agreement with KHK and from a government grant. In addition, we have borrowed under a secured term loan from Hercules (Hercules loan) to fund our operations. More particularly, since our inception and through December 31, 2013, we have raised an aggregate of $140.5 million to fund our operations, of which $110.5 million was from the sale of preferred stock and convertible debt securities (including $3.0 million from a bridge loan financing that closed

in June 2013 (2013 bridge note financing), $17.5 million was through our collaboration and license agreement with KHK, $0.5 million was from a federal government

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grant for our Qualifying Therapeutic Discovery Project in November 2010 and $12.0 million was from borrowings under the Hercules loan. As of December 31, 2013, our cash and cash equivalents were $46.6 million and we also had $0.3 million in assets held in restriction.

On February 4, 2014, we completed the initial public offering of our common stock, in which we issued and sold a total of 6,900,000 shares of common stock, including 900,000 shares sold pursuant to the exercise in full by the underwriters of an option to purchase additional shares, at a public offering price of $15.00 per share. We received net proceeds of approximately $92.9 million after deducting the underwriting commissions and discounts and offering expenses payable by us. All of the shares of our preferred stock were converted into shares of common stock and our warrants to purchase preferred stock became exercisable to purchase common stock immediately prior to the completion of our initial public offering.

Since inception, we have incurred significant operating losses. Our net loss was $8.6 million, $10.1 million and $18.5 million for the years ended December 31, 2011, 2012 and 2013, respectively. Substantially all of our operating losses resulted from expenses incurred in connection with our research programs and from general and administrative costs associated with our operations. We recognized revenue of $7.9 million and $7.0 million for the years ended December 31, 2011 and 2012, respectively, and no revenue was recognized for the twelve months ended December 31, 2013. Our revenue to date has been generated through our research collaboration and license agreement with KHK and a government grant. We have not generated any commercial product revenue. As of December 31, 2013, we had an accumulated deficit of $85.5 million. We expect to continue to incur significant and increasing losses in the foreseeable future. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially as we:

- advance our product candidates into preclinical development;
- conduct any clinical trials of DCR-PH1, DCR-M1711 and other potential product candidates;
- continue our research and development efforts, including to expand our pipeline and to enhance our technology platform;
- increase research and development related activities for the discovery and development of additional product candidates;
- manufacture clinical study materials and develop large-scale manufacturing capabilities;
- seek regulatory approval for our product candidates that successfully complete clinical trials;
- maintain, expand and protect our intellectual property portfolio;

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

operate as a public company.

We do not expect to generate substantial revenue from product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our product candidates, which is subject to significant uncertainty and which we expect will take at least seven years. If we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Until such time, if ever, that we generate product revenue, we expect to finance our cash needs through a combination of public or private equity offerings, debt financings and research collaboration and license agreements. We may be unable to raise capital or enter into such other arrangements when needed or on favorable terms. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop our product candidates.

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Collaboration agreement

In December 2009, we entered into a research collaboration and license agreement with KHK for the research, development and commercialization of DsiRNA molecules and drug delivery technologies for therapeutic targets in oncology. We have granted KHK an exclusive, worldwide, royalty-bearing and sub-licensable license to our DsiRNA molecules and drug delivery technologies and intellectual property for certain selected DsiRNA-based compounds. Under the research collaboration and license agreement, KHK is responsible for activities to develop, manufacture and commercialize the selected DsiRNA-based compounds and pharmaceutical products containing such compounds. For the KRAS product candidate, we have an option to co-promote in the U.S. for an equal share of the profits from U.S. net sales. In addition, for each product candidate under the research collaboration and license agreement, we have the potential to receive clinical, regulatory and commercialization milestone payments of up to $110.0 million and royalties on net sales of such product candidate.

Since the initiation of the research collaboration and license agreement, of the various targets in the collaboration, two target programs, including the initial target KRAS, have been nominated by KHK for formal development studies. Both programs utilize our specific RNAi-inducing double-stranded DsiRNA molecules and a lipid nanoparticle drug delivery technology proprietary to KHK. As of December 31, 2013, we have received total payments of $17.5 million from KHK under the research collaboration and license agreement.

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

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

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

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

Financial Operations Overview

Revenue

Our revenue to date has been generated primarily through research funding, license fees, option exercise fees and preclinical development payments under our research collaboration and license agreement with KHK and a government grant. We have not generated any commercial product revenue. For each product candidate under our research collaboration and license agreement with KHK, we are also entitled to receive clinical, regulatory and commercialization milestone payments of up to $110.0 million and royalties on net sales of such product candidate. We did not receive any royalty payments as of December 31, 2013.

The following table summarizes the sources of our revenue for the years ended December 31, 2011, 2012 and 2013 (in thousands).

	TWELVE MONTHS ENDED		
	DECEMBER 31, 2011	DECEMBER 31, 2012	DECEMBER 31, 2013
License fee and research funding	$ 2,500	$	$
Option exercise fees and preclinical payments	5,038	6,461	
Mutually agreed upon research	370	554	
Total	$ 7,908	$ 7,015	$

In the future, we may generate revenue from a combination of research and development payments, license fees and other upfront payments, milestone payments, product sales and royalties in connection with our collaboration with KHK or future collaborations and licenses. We expect that any revenue we generate will fluctuate in future periods as a result of the timing of our or a collaborator s achievement of preclinical, clinical, regulatory and commercialization milestones, if at all, the timing and amount of any payments to us relating to such milestones and the extent to which any of our product candidates are approved and successfully commercialized by us or a collaborator. If we, KHK or any future collaborator fails to develop product candidates in a timely manner or obtain regulatory approval for them, our ability to generate future revenue, and our results of operations and financial position, would be materially adversely affected.

Research and development expenses

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

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

platform-related lab expenses, including lab supplies, license fees and costs of 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.

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We expense research and development costs as they are incurred. We account for nonrefundable advance payments for goods and services that will be used in future research and development activities as expenses when the service has been performed or when the goods have been received. A significant portion of our research and development costs are not tracked by project as they benefit multiple projects or our technology platform and because none of our programs are in clinical development.

The following table summarizes our research and development expenses incurred during the years ended December 31, 2011, 2012 and 2013 (in thousands).

	TWELVE MONTHS ENDED		
	DECEMBER 31, 2011	DECEMBER 31, 2012	DECEMBER 31, 2013
Direct research and development expenses	$ 312	$ 1,315	$ 4,164
Platform-related expenses	5,948	5,931	3,492
Employee-related expenses	3,445	3,264	2,871
Facilities, depreciation and other expenses	1,000	1,055	1,031
Total	$ 10,705	$ 11,565	$ 11,558

We expect our research and development expenses to increase for the foreseeable future as we advance our product candidates toward preclinical studies and clinical trials. The process of conducting preclinical studies and clinical trials necessary to obtain regulatory approval is costly and time-consuming. We, KHK or any future collaborator may never succeed in obtaining marketing approval for any of our product candidates. The probability of success for each product candidate may be affected by numerous factors, including preclinical data, clinical data, competition, manufacturing capability and commercial viability.

All of our research and development programs are at an early stage and successful development of future product candidates from these programs is highly uncertain and may not result in approved products. Completion dates and completion costs can vary significantly for each future product candidate and are difficult to predict. We anticipate we will make determinations as to which product candidates to pursue and how much funding to direct to each product candidate on an ongoing basis in response to our ability to maintain or enter into collaborations with respect to each product candidate, the scientific and clinical success of each product candidate as well as ongoing assessments as to the commercial potential of product candidates. We will need to raise additional capital and may seek additional collaborations in the future in order to advance our various product candidates. Additional private or public financings may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a material adverse effect on our financial condition and our ability to pursue our business strategy.

General and administrative expenses

General and administrative expenses consist primarily of salaries and related benefits, including stock-based compensation, related to our executive, finance, legal, business development and support functions. Other general and administrative expenses include travel expenses, professional fees for auditing, tax and legal services and allocated facility-related costs not otherwise included in research and development expenses.

The following table summarizes our general and administrative expenses incurred during the years ended December 31, 2011, 2012 and 2013 (in thousands).

	TWELVE MONTHS ENDED		
	DECEMBER 31, 2011	DECEMBER 31, 2012	DECEMBER 31, 2013
General and administrative expenses	$ 4,816	$ 4,700	$ 5,820

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

Interest income

Interest income consists of interest income earned on our cash and cash equivalents.

Interest expense

Interest expense consists of interest expense on our borrowings under bridge financing loans that converted into shares of our preferred stock (convertible notes), including our 2013 bridge notes financing and the Hercules loan.

Preferred stock warrant remeasurement

Preferred stock warrant remeasurement is associated with warrants to purchase preferred stock issued to lenders under our convertible notes and the Hercules loan. The remeasurement consists of the change in value calculated using the Black-Scholes option pricing model to estimate the fair value of the warrants. We base the estimates in the Black-Scholes option pricing model, in part, on subjective assumptions, including stock price volatility, risk-free interest rate, dividend yield and the fair value of the preferred stock underlying the warrants. The remeasurement gain or loss associated with the change in the fair value of the preferred stock warrant liability each reporting period is recognized as a component of other income (expense). Upon the completion of our initial public offering on February 4, 2014, the preferred stock warrant liability was reclassified as a component of equity and is no longer subject to remeasurement.

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. (GAAP). The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the revenue and expenses incurred during the reported periods. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued expenses, revenue recognition, deferred revenue and stock-based compensation. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ from these estimates under different assumptions or conditions.

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

Collaborative research and development and multiple-deliverable arrangements

We have generated our revenue primarily through our research collaboration and license agreement with KHK and a government grant. The terms of the research collaboration and license agreement with KHK include multiple deliverables by us (e.g., license rights and research and development services) in exchange for consideration to us of

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some combination of research funding, license fees, option exercise fees, payments based upon the achievement of specified milestones and royalty payments based on product sales derived from the collaboration.

We recognize revenue when all of the following four criteria are met: (1) persuasive evidence that an arrangement exists; (2) delivery of the products or services has occurred; (3) the selling price is fixed or determinable; and (4) collectibility is reasonably assured. Multiple-deliverable arrangements, such as license and development agreements, are analyzed to determine whether the deliverables can be separated or whether they must be accounted for as a single unit of accounting. When deliverables are separable, consideration received is allocated to the separate units of accounting based on the relative selling price method and the appropriate revenue recognition principles are applied to each unit. When we determine that an arrangement should be accounted for as a single unit of accounting, we must determine the period over which the performance obligations will be performed and revenue will be recognized.

At the inception of each arrangement that includes payments for optional research or milestones, we evaluate whether each option or milestone is substantive and at risk to both parties on the basis of the contingent nature of the option or milestone. This evaluation includes an assessment of whether: (1) the consideration is commensurate with either the entity s performance to achieve the milestone or the enhancement of the value of the delivered items; (2) as a result of a specific outcome resulting from the entity s performance to achieve the milestone; (3) the consideration relates solely to past performance; and (4) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. Substantive options and milestones are recognized as revenue upon the achievement of the milestone, assuming all other revenue recognition criteria are met.

License fees are initially recorded as deferred revenue upon receipt and then recognized as revenue over our performance period. 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 costs in the period in which it is incurred. Assuming all other revenue recognition criteria are met, milestone payments are recognized as revenue when the milestone is achieved or is probable of achievement. Royalty payments are recognized as revenue based on contract terms and reported sales of licensed products, when reported sales are reliably measurable and collectability is reasonably assured.

As part of our collaboration agreement with KHK, we have an option to co-promote the KRAS product candidate in the U.S. for an equal share of the profits from U.S. net sales.

Preferred stock warrants liability

As of December 31, 2013, we had outstanding warrants for the purchase of shares of Series A and Series B preferred stock as well as warrants issued in the Series C bridge loan that became exercisable for shares of Series C preferred stock upon the closing of our sale of Series C preferred stock in July 2013 (Series C warrants). We account for freestanding warrants related to shares that are redeemable or contingently redeemable, or for purchases of preferred stock that are not indexed to our stock, as liabilities. The warrants are recorded at fair value, estimated using the Black-Scholes option-pricing model, at each balance sheet date with changes in the fair value of the liability recorded in the statement of operations.

Pursuant to the terms of these warrants, upon the conversion of the class of preferred stock underlying the warrant, the warrants automatically become exercisable for shares of our common stock based upon the conversion ratio of the underlying class of preferred stock. The consummation of our initial public offering resulted in the conversion of all classes of our preferred stock into common stock. Upon the conversion of the underlying classes of preferred stock, our outstanding warrants to purchase Series A, Series B and Series C preferred stock were reclassified as a component

of equity and are no longer subject to remeasurement.

Net operating loss and research and development tax credit carryforwards

We file U.S. federal income tax returns and Massachusetts state tax returns. The deferred tax assets were primarily comprised of federal and state tax net operating losses and tax credit carryforwards and were recorded

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using enacted tax rates expected to be in effect in the years in which these temporary differences are expected to be utilized. As of December 31, 2013, the Company has approximately $65.1 million of federal and $64.6 million of state net operating loss carryforwards, and $1.1 million of federal and 0.7 million of Massachusetts research and development credits that expire starting in 2028. As of December 31, 2013, we had $0.9 million of unrecognized tax benefits, of which $0.9 million would affect income tax expense if recognized, before consideration of our valuation allowance.

Utilization of the net operating loss and tax credit carryforwards may be subject to an annual limitation due to historical or future ownership percentage change rules provided by the Internal Revenue Code of 1986, as amended, and similar state provisions. The annual limitation may result in the expiration of certain net operating loss and tax credit carryforwards before their utilization. However, due to uncertainties surrounding our ability to generate future taxable income to realize these tax assets, a full valuation allowance has been established to offset our deferred tax assets.

Redeemable convertible preferred stock

We have issued preferred stock in the past to raise capital. We initially record preferred stock redeemable outside of our control outside of stockholders deficit at the value of the proceeds received or fair value, if lower, net of issuance costs. Subsequently, if it is probable that the preferred stock will become redeemable, we adjust the carrying value to the redemption value over the period from the issuance date to the earliest possible redemption date.

Stock-based compensation and common stock valuation

Stock-based compensation

We estimate the fair value of our stock-based awards to employees and non-employees using the Black-Scholes option-pricing model, which requires the input of highly subjective assumptions, including: (1) the expected volatility of our stock, (2) the expected term of the award, (3) the risk-free interest rate and (4) expected dividends. Due to the lack of a public market for the trading of our common stock before the completion of our initial public offering and a lack of company specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. For these analyses, we have selected companies with comparable characteristics to ours, including enterprise value, risk profiles, position within the industry and historical share price information, sufficient to meet the expected life of the stock-based awards. We compute the historical volatility data using the daily closing prices for the selected companies shares during the equivalent period of the calculated expected term of our stock-based awards. We have estimated the expected life of our employee stock options using the simplified method, whereby the expected life equals the average of the vesting term and the original contractual term of the option. The risk-free interest rates for periods within the expected life of the option are based on the U.S. Treasury yield curve in effect during the period the options were granted.

We are also required to estimate forfeitures at the time of grant and revise those estimates in subsequent periods if actual forfeitures differ from estimates. We use historical data to estimate pre-vesting option forfeitures and record stock-based compensation expense only for those awards that are expected to vest. Stock-based compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest.

Common stock valuations

We have historically granted stock options at exercise prices not less than the fair value of our common stock. As there was no public market for our common stock before our initial public offering, the estimated fair value of our

common stock was previously determined by our board of directors. We have periodically determined, for financial reporting purposes, the estimated per share fair value of our common stock at various dates using contemporaneous valuations performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities*

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Issued as Compensation (Practice Aid). We performed these contemporaneous valuations as of January 31, 2012 and August 31, 2013. In conducting the contemporaneous valuations, we considered all objective and subjective factors that we believed to be relevant for each valuation conducted, including our best estimate of our business condition, prospects and operating performance at each valuation date. Within the contemporaneous valuations performed, a range of factors, assumptions and methodologies were used. The significant factors included:

- the prices of our preferred stock sold to or exchanged between outside investors in arm s length transactions, and the rights, preferences and privileges of our preferred stock as compared to those of our common stock, including the liquidation preferences of our preferred stock;
- our results of operations, financial position and the status of research and development efforts;
- the composition of, and changes to, our management team and board of directors;
- the lack of liquidity of our common stock as a private company;
- our stage of development and business strategy and the material risks related to our business and industry;
- the achievement of enterprise milestones, including entering into collaboration and license agreements;
- the valuation of publicly traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of peer companies;
- any external market conditions affecting the life sciences and biotechnology industry sectors;
- the likelihood of achieving a liquidity event for the holders of our common stock and stock options, such as an initial public offering or a sale of our company, given prevailing market conditions;
- the state of the initial public offering market for similarly situated privately held biotechnology companies; and
- any recent contemporaneous valuations prepared by our board of directors and management in accordance with methodologies outlined in the Practice Aid.

Stock option grants on December 4, 2013 and December 30, 2013

For the stock options granted by us on December 4, 2013 and December 30, 2013, our board of directors determined that the fair value of common stock of $3.42 per share calculated in the contemporaneous valuation as of August 31, 2013 reasonably reflected the per share fair value of our common stock on each of the grant dates. However, in the context and given the anticipated proximity of our initial public offering, for financial reporting purposes, in early January 2014 we conducted a retrospective valuation as of December 31, 2013, which reasonably assumed that examination of contemporaneous information would have concluded a price range consistent with the then estimated price range for our initial public offering of $11.00 to $13.00 per share. The retrospective valuation concluded that, with such contemporaneous information, the fair value of our common stock as of December 31, 2013 was $7.42 per share primarily due to feedback from investment bankers that we had an increased probability of executing a successful initial public offering in the first quarter of 2014 and feedback from investment bankers that public investors could potentially price our common stock in the range of $11.00 to $13.00 per share in such an initial public offering. Accordingly, we recognized a stock-based compensation charge of less than $0.1 million in relation to the December 4, 2013 and December 30, 2013 option grants for the quarter ended December 31, 2013 based on the grant date fair value of our common stock as determined by the retrospective valuation.

Emerging growth company status

In April 2012, the Jumpstart Our Business Startup Act (JOBS Act) was enacted by the federal government. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period for complying with new or revised accounting standards. Thus, an emerging growth company

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can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

Recent Accounting Pronouncements

There are no recent accounting standards that would impact our results reported or in the consolidated financial statements included in this report.

Comparison of the years ended December 31, 2012 and 2013

The following table summarizes the results of our operations for the years ended December 31, 2012 and 2013 (in thousands, except percentages):

	FOR THE TWELVE MONTHS ENDED DECEMBER 31,		INCREASE (DECREASE)	
	2012	2013		
Revenue:				
License fee and research funding	$	$	$	0%
Option exercise fees and preclinical payments	6,461		(6,461)	(100)%
Mutually agreed upon research	554		(554)	(100)%
Total revenue	7,015		(7,015)	(100)%
Expenses:				
Research and development	11,565	11,558	(7)	0%
General and administrative	4,700	5,820	1,120	24%
Total expenses	16,265	17,378	1,113	7%
Loss from operations	(9,250)	(17,378)	(8,128)	(88)%
Other expense	871	1,140	269	31%
Net loss	$ (10,121)	$ (18,518)	$ (8,397)	(83)%

Revenue

We recognized revenue of $7.0 million for the twelve months ended December 31, 2012 and no revenue for the twelve months ended December 31, 2013. The revenue recognized during the twelve months ended December 31, 2012 related to portions of an option exercise fee and mutually agreed upon research received as part of the research collaboration and license agreement with KHK. No revenue producing events occurred during the twelve months ended December 31, 2013. We do not expect to generate any product revenue for the foreseeable future.

Research and development expenses

Research and development expenses were $11.6 million for the twelve months ended December 31, 2012 and $11.6 million for the twelve months ended December 31, 2013. The employment-related expenses for the twelve months ended December 31, 2012 decreased by $0.4 million compared to the twelve months ended December 31, 2012 due to a realignment and reduction of staff in 2013 and the spending on research and development of DsiRNA molecules and delivery technologies for the twelve months ended December 31, 2013 decreased by $2.4 million compared to the twelve months ended December 31, 2012, both of which were offset by a $2.8 million increase in DCR-M1711 project-related expenses due to a natural shift of resources from our EnCore platform towards increased development activities in preparation for a clinical trial for DCR-M1711 that

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we expect to initiate in the first half of 2014. We expect our research and development expenses to increase in 2014 as we continue spending on our development programs.

General and administrative expenses

General and administrative expenses were $4.7 million for the twelve months ended December 31, 2012 and $5.8 million for the twelve months ended December 31, 2013. The increase of $1.1 million, or 24 percent compared to the twelve months ended December 31, 2012, was primarily due to a $0.6 million increase in employee-related expenses and a $0.5 million increase in professional fees indirectly related to the initial public offering of our common stock. We expect general and administrative expenses to increase in the future as we expand our operating activities and incur additional costs associated with being a publicly-traded company.

Other expense

Other expense was $0.9 million for the twelve months ended December 31, 2012 and $1.1 million for the twelve months ended December 31, 2013. The increase of $0.2 million, or 31 percent compared to the twelve months ended December 31, 2012, was primarily due to the loss on extinguishment of debt in 2013 of $0.3 million and a decrease in expense related to the remeasurement of the warrants exercisable for Series A, Series B and Series C preferred stock of $0.3 million, which were partially offset by a decrease of interest expense by $0.4 million. The loss on extinguishment relates to the 2013 bridge note financing that closed in June 2013. The decrease in interest expense was due to a decrease in the Hercules loan balance outstanding at December 31, 2013 as compared to December 31, 2012. We expect interest expense to continue to decrease commensurate with decreases in the Hercules loan principle balance outstanding, on which we intend to continue to make installment payments with the intent of repaying the Hercules loan in full in January 2015.

Comparison of the twelve months ended December 31, 2011 and 2012

The following table summarizes the results of our operations for the twelve months ended December 31, 2011 and 2012 (in thousands, except percentages):

	FOR THE TWELVE MONTHS ENDED DECEMBER 31,		INCREASE (DECREASE)	
	2011	2012		
Revenue:				
License fee and research funding	$ 2,500	$	$ (2,500)	(100)%
Option exercise fees and preclinical payments	5,038	6,461	1,423	28%
Mutually agreed upon research	370	554	184	50%
Total revenue	7,908	7,015	(893)	(11)%
Expenses:				
Research and development	10,705	11,565	860	8%
General and administrative	4,816	4,700	(116)	(2)%
Total expenses	15,521	16,265	744	5%
Loss from operations	(7,613)	(9,250)	(1,637)	22%

Other expense	943	871	(72)	(8)%
Net loss	$ (8,556)	$ (10,121)	$ (1,565)	(18)%

Revenue

We recognized revenue of $7.9 million for the twelve months ended December 31, 2011 and $7.0 million for the twelve months ended December 31, 2012. Total revenue in both years relates to payments received under

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our research collaboration and license agreement with KHK. Research funding and license fees revenue recognized in 2011 related to revenue earned over the original term of the collaboration and research license agreement of two years. The increase in the option exercise fees and preclinical payments was primarily due to the satisfaction of certain preclinical development criteria that were satisfied in 2012.

The decrease of $0.9 million, or 11 percent, was primarily due to reductions in revenue from license fee and research funding of $2.5 million, which were partially offset by the increase in option exercise fees and preclinical development payments of $1.4 million in 2012 and a small increase in mutually agreed upon research revenue of $0.2 million.

Research and development expenses

Research and development expenses were $10.7 million for the twelve months ended December 31, 2011 and $11.6 million for the twelve months ended December 31, 2012. The increase of $0.9 million, or 8 percent, was primarily due to a $1.0 million increase in spending on DCR-M1711 project to support increased development activities in preparation for a clinical trial planned to commence in the first half of 2014, offset by a $0.1 million net decrease in indirect research and development expenses.

General and administrative expenses

General and administrative expenses were $4.8 million for the twelve months ended December 31, 2011 and $4.7 million for the twelve months ended December 31, 2012. The decrease of $0.1 million, or 2 percent, was primarily due to a decrease in outside legal fees of $0.2 million, partially offset by an increase in payroll-related expenses of $0.1 million.

Other expense

Interest and other income were approximately $1.0 million for the twelve months ended December 31, 2011 and $0.9 million for the twelve months ended December 31, 2012. The decrease of $0.1 million, or 10 percent compared to the twelve months ended December 31, 2012 was primarily due to $0.4 million of income resulting from a greater decrease in the fair market value of the warrants for Series A preferred stock and Series B preferred stock in 2012 of $0.5 million compared to $0.1 million in 2011. This income was partially offset by an increase in interest expense of $0.3 million, or 30 percent resulting from a $5.0 million increase in the Hercules loan balance outstanding in the fourth quarter of 2011.

Liquidity and Capital Resources

Since our inception and through December 31, 2013, we have raised an aggregate of $140.5 million to fund our operations, of which $110.5 million was from the sale of preferred stock and convertible debt securities (including $3.0 million from the 2013 bridge note financing), $17.5 million was through our collaboration and license agreement with KHK, $0.5 million was from a federal government grant for our Qualifying Therapeutic Discovery Project in November 2010 and $12.0 million was from borrowings under the Hercules loan. As of December 31, 2013, our cash and cash equivalents were $46.6 million and we also had $0.3 million in assets held in restriction.

On February 4, 2014, we closed our initial public offering, in which we issued and sold a total of 6,900,000 shares of our common stock, including 900,000 shares sold pursuant to the exercise in full by the underwriters of their option to purchase additional shares, at a public offering price of $15.00 per share, and received net proceeds of approximately $92.9 million after deducting underwriting commissions and discounts and offering expenses payable by us.

In June 2011, we entered into an amendment to our original loan and security agreement with Hercules, pursuant to which we are entitled to borrow a term loan in the principal amount of up to $12.0 million with a

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floating interest rate equal to the greater of (1) 10.15 percent or (2) the sum of 10.15 percent plus the prime rate published on The Wall Street Journal minus 5.75 percent, not to exceed 12.75 percent per annum, which interest is computed daily based on the actual number of days elapsed. The interest is payable monthly and the principal amount is payable in equal monthly installments beginning April 1, 2012 through January 2, 2015. We granted Hercules a security interest in certain of our assets. In connection with the loan and security agreement, as amended, we issued to Hercules warrants to purchase 21,000 shares of Series A preferred stock and 26,400 shares of Series B preferred stock, respectively, each at an exercise price of $25.00 per share. The warrants became exercisable to purchase our common stock immediately prior to the closing of our initial public offering.

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

Cash flows

As of December 31, 2013, we had $46.6 million in cash and cash equivalents and $0.3 million in assets held in restriction as well as $5.0 million in indebtedness. The indebtedness represents the aggregate principal amount under our secured term loan.

The following table shows a summary of our cash flows for the years ended December 31, 2011, 2012 and 2013 (in thousands).

	FOR THE TWELVE MONTHS ENDED DECEMBER 31,		
	2011	**2012**	**2013**
Net cash used in operating activities	$ (8,866)	$ (15,737)	$ (10,944)
Net cash used in investing activities	(501)	(120)	(413)
Net cash provided by (used in) financing activities	7,255	(2,963)	54,282
Increase (decrease) in cash and cash equivalents	$ (2,112)	$ (18,820)	$ 42,925

Operating activities

Net cash used in operating activities was $15.7 million and $10.9 million for the years ended December 31, 2012 and 2013. The decrease in cash used in operating activities of $4.8 million was primarily due to a decrease in our research collaboration and license agreement receivable of $5.0 million for the twelve months ended December 31, 2013 related to an option exercise fee and preclinical payments earned in December 2012 but not collected until 2013, which was partially offset by an increase in working capital and other non-cash items of $0.2 million for the twelve months ended December 31, 2013.

Net cash used in operating activities was $8.9 million and $15.7 million for the years ended December 31, 2011 and 2012. The increase in cash used in operating activities of $6.8 million was primarily due to an increase in net loss by $1.6 million compared to 2012 and an increase in our research and license agreement receivable compared to 2012. The increase in net loss resulted mostly from a decrease in revenue from KHK and an increase in research and

development spending on DCR-M1711. The increase in our research and license agreement receivable related primarily to a preclinical payment of $5.0 million earned in December 2012 but not collected until 2013.

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Investing activities

Net cash used in investing activities for the periods presented relates entirely to purchases of property and equipment, mostly laboratory equipment. Net cash used in investing activities was $0.1 million and $0.4 million for the years ended December 31, 2012 and 2013. Net cash used in investing activities for the years ended December 31, 2011 and 2012 was $0.5 million and $0.1 million, respectively.

Financing activities

Net cash used in financing activities of $3.0 million for the twelve months ended December 31, 2012 relates entirely to repayments on the Hercules loan. Net cash provided by financing activities of $54.3 million for the twelve months ended December 31, 2013 is due to $60.0 million of proceeds from the issuance of Series C preferred stock (including $3.0 million of proceeds received in our 2013 bridge note financing for the purchase of convertible promissory notes and Series C warrants), which is partially offset by $4.1 million of repayments on the Hercules loan and $1.6 million of issuance costs.

Net cash provided by financing activities of $7.3 million for the twelve months ended December 31, 2011 is primarily due to $8.6 million of proceeds resulting from an amendment to increase our borrowings under the Hercules loan, which is partially offset by $1.4 million of repayments on that loan. Net cash used in financing activities of $3.0 million for the twelve months ended December 31, 2012 relates entirely to repayments on our Hercules loan.

Funding requirements

We expect that our primary uses of capital will continue to be third-party clinical research and development services, compensation and related expenses, laboratory and related supplies, legal and other regulatory expenses and general overhead costs. We believe that the net proceeds of approximately $92.9 million received in our initial public offering, together with our existing cash and cash equivalents as of December 31, 2013, but excluding any potential option exercise fees or milestone payments, will be sufficient to meet our anticipated cash requirements through 2016. However, we may require additional capital for the further development of our existing product candidates and may also need to raise additional funds sooner to pursue other development activities related to additional product candidates.

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. 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 future capital requirements are difficult to forecast and will depend on many factors, including:

- the receipt of milestone payments under our research collaboration and license agreement with KHK;
- the terms and timing of any other collaboration, licensing and other arrangements that we may establish;
- the initiation, progress, timing and completion of preclinical studies and clinical trials for our potential product candidates;

the number and characteristics of product candidates that we pursue;

the progress, costs and results of our preclinical studies and clinical trials;

the outcome, timing and cost of regulatory approvals;

delays that may be caused by changing regulatory requirements;

the cost and timing of hiring new employees to support our continued growth;

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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 and timing of procuring clinical and commercial supplies of our product candidates;

the extent to which we acquire or in-license other product candidates and technologies; and

the extent to which we acquire or invest in other businesses, product candidates or technologies.

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.

Until such time, if ever, we generate product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings and research collaboration and license agreements. We may be unable to raise capital or enter into such other arrangements when needed or on favorable terms or at all. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop our product candidates.

Contractual Obligations and Commitments

The following is a summary of our significant contractual obligations as of December 31, 2013 (in thousands).

		PAYMENTS DUE BY PERIOD			
CONTRACTUAL OBLIGATIONS	TOTAL	LESS THAN 1 YEAR	MORE THAN 1 YEAR AND LESS THAN 3	MORE THAN 3 YEARS AND LESS THAN 5	MORE THAN 5 YEARS
Short and long-term debt obligations(1)	$ 5,025	$ 4,587	$ 438	$	$
Interest on short- and long-term debt obligations(2)	309	305	4		
Operating lease obligations(3)	1,772	579	1,193		
Total	$ 7,107	$ 5,471	$ 1,635	$	$

(1) Short and long-term debt obligations relate to principal payments due on our outstanding secured term loan.
(2) Projected estimated interest payments due on our outstanding secured term loan.
(3) Future minimum lease payments under our non-cancelable operating lease for our current office and lab space in Watertown, Massachusetts that, as amended on July 3, 2013, expires on November 30, 2016 with an average rent of approximately $51 per month.

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

Off-balance Sheet Arrangements

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

Segment Reporting

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

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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, 2011 and 2012 and 2013, we had cash and cash equivalents of $22.3 million, $3.7 million and $46.6 million, respectively, consisting of an interest-bearing money market account. 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 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. To minimize the risk in the future, we intend to maintain our portfolio of cash and cash equivalents and short-term investments in a variety of securities, including commercial paper, money market funds, government and non-government debt securities and corporate obligations.

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Item 8. ***Financial Statements and Supplementary Data***

DICERNA PHARMACEUTICALS, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of

Dicerna Pharmaceuticals, Inc.

Watertown, Massachusetts

We have audited the accompanying consolidated balance sheets of Dicerna Pharmaceuticals, Inc. and its subsidiary (the Company) as of December 31, 2013 and 2012, and the related consolidated statements of operations, redeemable convertible preferred stock and stockholders deficit, and cash flows for each of the three years in the period ended December 31, 2013. These financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, 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. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, such financial statements present fairly, in all material respects, the financial position of Dicerna Pharmaceuticals, Inc. and its subsidiary as of December 31, 2013 and 2012, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2013, in conformity with accounting principles generally accepted in the United States of America.

/s/ Deloitte & Touche LLP

Boston, Massachusetts

March 27, 2014

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DICERNA PHARMACEUTICALS, INC.

Consolidated Balance Sheets

As of December 31, 2012 and 2013

(In thousands, except share data and par value)

	DECEMBER 31,	
	2012	2013
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 3,670	$ 46,595
Research and license agreement receivable	5,018	
Prepaid expenses and other current assets	344	2,058
Total current assets	9,032	48,653
NONCURRENT ASSETS:		
Property and equipment net	883	877
Assets held in restriction	264	264
Other assets	12	
Total noncurrent assets	1,159	1,141
TOTAL ASSETS	$ 10,191	$ 49,794
LIABILITIES AND STOCKHOLDERS DEFICIT		
CURRENT LIABILITIES:		
Accounts payable	$ 1,198	$ 1,700
Current portion of long-term debt	4,140	