Dicerna Pharmaceuticals Inc
Form 10-K
March 30, 2017
Table of Contents

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

Form 10-K

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

For the fiscal year ended December 31, 2016

or

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

For the transition period from to

Commission File Number: 001-36281

DICERNA PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

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

87 Cambridgepark Drive Cambridge, MA 02140

(Address of principal executive offices and zip code)

(617) 621-8097

(Registrant s telephone number, including area code)

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

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

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

None

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

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

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405) is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information

statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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 (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

Based on the closing price of the registrant s Common Stock on the last business day of the registrant s most recently completed second fiscal quarter, which was June 30, 2016, the aggregate market value of its shares (based on a closing price of $3.00 per share) held by non-affiliates was approximately $39.3 million. Shares of the registrant s Common Stock held by each executive officer and director and by each entity or person that owned five percent or more of the registrant s outstanding Common Stock were excluded in that such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of March 29, 2017, there were 20,794,193 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s definitive proxy statement for its 2017 Annual Meeting of Stockholders are incorporated by reference into Part III hereof. Such proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

Table of Contents

DICERNA PHARMACEUTICALS, INC.

2016 ANNUAL REPORT ON FORM 10-K

TABLE OF CONTENTS

Table of Contents

Forward-Looking Statements

This Annual Report on Form 10-K includes forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, 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:

- our ability to obtain additional funds for our operations;
- the initiation, timing, progress and results of our research and development programs, preclinical studies, any clinical trials and Investigational New Drug (IND) application, New Drug Application (NDA) and other regulatory submissions;
- our ability to identify and develop product candidates for treatment of additional disease indications;
- our or a collaborator s ability to obtain and maintain regulatory approval of any of our product candidates;
- the rate and degree of market acceptance of any approved product candidates;
- the commercialization of any approved product candidates;
- our ability to establish and maintain additional collaborations and retain commercial rights for our product candidates in the collaborations;
- the implementation of our business model and strategic plans for our business, technologies and product candidates;
- our estimates of our expenses, ongoing losses, future revenue and capital requirements;
- our ability to obtain and maintain intellectual property protection for our technologies and product candidates and our ability to operate our business without infringing the intellectual property rights of others;
- our reliance on third parties to conduct our preclinical studies or any future clinical trials;

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

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

our dependence on our existing collaborator, Kyowa Hakko Kirin Co., Ltd. (KHK), for developing, obtaining regulatory approval for and commercializing product candidates in the collaboration;

our receipt and timing of any milestone payments or royalties under our research collaboration and license agreement with KHK or arrangement with any future collaborator;

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

our financial performance; and

developments relating to our competitors or our industry.

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

Table of Contents

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

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

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

Trademarks

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

Table of Contents

PART I

Item 1. ***Business***

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

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

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

Development Programs

In choosing which development programs to advance, we apply scientific, clinical, and commercial criteria that we believe allow us to best leverage our GalXC RNAi platform and maximize value. To date the Company has launched its efforts directed to four therapeutic programs: DCR-PHXC for the treatment of primary hyperoxaluria (PH) type 1 (PH1), DCR-PCSK9 for the treatment of hypercholesterolemia, DCR-HBV for the treatment of chronic hepatitis B virus (HBV) infection, and an additional program against an undisclosed rare disease. The Company has the capacity to launch up to three programs every year, and intends to advance five programs into the clinic by the end of 2019. We plan to file our first IND application and/or Clinical Trial Application (CTA) for our GalXC product candidates at the end of 2017, followed by additional INDs in 2018 and 2019.

Table of Contents

The table below sets forth the stage of development of our various product candidates as of March 29, 2017.

Our current development programs are as follows:

Primary Hyperoxaluria Type 1 (PH1). We are developing DCR-PHXC for the treatment of PH1. PH1 is a rare inborn error of metabolism in which the liver produces excessive levels of oxalate, which in turn causes damage to the kidneys and to other tissues in the body. In preclinical models of PH, DCR-PHXC reduces oxalate production to near-normal levels, ameliorating the disease condition. DCR-PHXC is in preclinical development, and has advanced into IND-enabling studies. We plan to file an IND submission and/or CTA for DCR-PHXC in late 2017 and commence human clinical trials in the first quarter of 2018.

To facilitate DCR-PHXC development, we continue to advance our Primary HYperoxaluria Observational Study (PHYOS), an international, multicenter, observational study in patients with a genetically confirmed diagnosis of PH1. PHYOS is collecting data on key biochemical parameters implicated in the pathogenesis of PH1. We hope to use the data to better understand the baseline PH1 disease state, which will help guide long-term drug development plans.

In the third quarter of 2016, we announced that we had transitioned our PH1 program to DCR-PHXC from DCR-PH1, a lipid nanoparticle (LNP) formulated RNAi compound. DCR-PH1 was being studied in two clinical trials, DCR-PH1-101 in patients with PH1 and DCR-PH1-102 in normal healthy volunteers (NHVs). Both studies have been discontinued, and in November 2016, our licensing and collaboration agreement with Arbutus Biopharma Corporation (formerly Tekmira Pharmaceuticals Corporation) (Arbutus) to license Arbutus LNP delivery technology for exclusive use in our PH1 development program terminated in accordance with its terms.

We presented initial data from the NHV study at the 17th Congress of the International Pediatric Nephrology Association (IPNA) in Iguaçu, Brazil on September 22, 2016. We believe these data provide the proof of concept for the pharmacological activity of RNAi-based therapy in PH1.

Hypercholesterolemia (PCSK9 targeted therapy). We are using our GalXC RNAi platform to develop a therapeutic that targets the proprotein convertase subtilisin/kexin type 9 (PCSK9) gene for the treatment of hypercholesterolemia. Based on the Company s candidate development work during the fourth quarter of 2016, Dicerna is positioned to advance DCR-PCSK9, which targets the PCSK9 gene and is indicated for the treatment of statin-refractory patients with hypercholesterolemia, into formal preclinical development. PCSK9 is a validated target for hypercholesterolemia, and there are United States (U.S.) Food and Drug Administration (FDA)-approved therapies targeting PCSK9 that are based on monoclonal antibody (MAb) technology. Based on preclinical studies, we believe that our GalXC RNAi platform can produce a PCSK9-targeted therapy with more attractive commercial

STAGES OF DEVELOPMENT PRODUCT CANDIDATE INDICATION RESEARCH PRECLINICAL CLINICAL POC STUDIES DCR-PHXC Primary Hyperoxaluria Undisclosed Rare Disease DCR-PCSK9 Cardiovascular Disease DCR-HBV Hepatitis B Virus Undisclosed Cardiovascular Disease Undisclosed Chronic Liver Disease Our

Table of Contents

properties than existing MAb therapies, based on comparatively smaller subcutaneous injection volumes and less frequent dosing, while providing equal or superior control of serum cholesterol.

An undisclosed rare disease involving the liver. We are developing a GalXC-based therapeutic, targeting a liver-expressed gene involved in a serious rare disease. For competitive reasons we have not yet publicly disclosed the target gene or disease. We have selected this target gene and disease based on criteria that include having a strong therapeutic hypothesis, a readily-identifiable patient population, the availability of a potentially predictive biomarker, high unmet medical need, favorable competitive positioning, and what we believe is a rapid projected path to approval. We plan to file an IND and/or CTA for this program in the second quarter of 2018.

Chronic Hepatitis B Virus infection: Based on our candidate development work during the fourth quarter of 2016, we are positioned to advance DCR-HBV, which targets the HBV directly, into formal preclinical development. We are using our GalXC RNAi platform to investigate potential pharmaceutical treatments for HBV. Current therapies for HBV rarely lead to a long-term immunological cure as measured by the clearance of HBV surface antigen (HBsAg) and sustained HBV deoxyribonucleic acid (DNA) suppression. Based on preclinical studies, we believe that our GalXC RNAi platform can produce an experimental HBV-targeted therapy that eliminates HBsAg expression in HBV patients and that has the potential to be delivered in a commercially attractive subcutaneous dosing paradigm.

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

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

Strategy

We are committed to delivering transformative therapies based on our GalXC RNAi platform to patients with rare inherited diseases involving the liver and for other therapeutic areas involving the liver such as chronic liver diseases, cardiovascular diseases, and viral infectious diseases. We have qualified dozens of disease-associated genes in clinical indications where we believe an RNAi-based inhibitor may provide substantial benefit to patients, providing expansive therapeutic opportunities. In addition, Dicerna has developed hits and/or optimized GalXC conjugate inhibitors against almost 40 of these qualified targets.

The key elements of our strategy are as follows.

Create new programs in indication areas with high unmet medical need. We intend to continue to use our proprietary GalXC RNAi technology platform to create new, high value pharmaceutical programs. Our primary focus will remain: (1) rare inherited diseases involving the liver; and (2) other therapeutic areas involving the liver such as chronic liver diseases, cardiovascular diseases, and viral infectious diseases.

Table of Contents

Validate our product candidates and our platform in clinical proof-of-concept studies. We believe data from the DCR-PH1-102 clinical trial in NHVs provide the proof of concept for the pharmacological activity of RNAi-based therapy in PH1. We intend to demonstrate clinical proof-of-concept for DCR-PHXC (which focuses on the treatment of PH1 as well) and for our other development programs. Based on precedents in the RNAi field, we are optimistic that our preclinical data showing the significant knockdown of target mRNA activity lasting for up to three months after the last dose and disease biomarker activity, may translate into clinical results for these programs.

Retain significant portions of the commercial rights for certain rare disease programs. We seek to retain a full or substantial ownership stake and invest internally in disease areas with focused patient populations, such as certain rare diseases, as we see such diseases representing opportunities that carry high probabilities of success, have easily identifiable patient populations and a limited number of Centers of Excellence to facilitate reaching these patients, and have the potential for more rapid clinical development programs. For more complex diseases with multiple gene dysfunctions and larger patient populations, we plan to pursue partnerships that can provide the enhanced scale, resources and commercial infrastructure required to maximize these prospects.

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

Continue to invest in our RNAi technology platform and intellectual property. We plan to continue to invest in expanding and improving our GalXC RNAi platform technology. We believe we have a robust patent portfolio covering our proprietary GalXC RNAi platform and other RNAi technologies. As of March 29, 2017, our patent estate, not including the patents and patent applications we have licensed, included over 20 issued patents or allowed patent applications and over 100 pending patent applications supporting commercial development of our RNAi molecules and delivery technologies.

Leverage the experience and the expertise of our executive management team. To execute on our strategy, we have assembled an executive management team that has extensive experience in the biopharmaceutical industry. In addition, various members of our management team and our board of directors have contributed to the progress of the RNAi field through their substantial involvement in companies such as Cephalon Inc., Genta Inc., GlaxoSmithKline plc, Pfizer Inc., Sanofi, Sirna Therapeutics, Inc. (Sirna), and other companies. Our co-founder and chief executive officer, Douglas M. Fambrough III, Ph.D., was a lead venture capital investor and board member of Sirna, an early RNAi company acquired by Merck & Co., Inc. (Merck) in 2006 for $1.1 billion.

Recent Developments

On March 30, 2017, we entered into a redeemable convertible preferred stock purchase agreement (SPA) with seven institutional investors (Investors), led by funds advised by Bain Capital Life Sciences L.P. (Lead Investor), pursuant to which we agreed to issue and sell in a private placement 700,000 shares of our newly designated Redeemable

Convertible Preferred Stock, par value $0.0001 per share (Redeemable Convertible Preferred), at a purchase price of $100.00 per share, for total gross proceeds of $70.0 million (Private Placement). Other participants in the financing include EcoR1 Capital, Cormorant Asset Management, RA Capital, Domain Associates and Skyline Ventures, among others. The Private Placement is expected to close on or before April 11, 2017, subject to the satisfaction of customary closing conditions.

We plan to file a Certificate of Designation of Redeemable Convertible Preferred Stock (Certificate of Designation) with the Secretary of State of the State of Delaware establishing that each share of Redeemable Convertible Preferred will have a stated value of $100.00 (Stated Value). Pursuant to the Certificate of Designation, we shall have the right to require the Investors to convert the Redeemable Convertible Preferred

Table of Contents

into common stock (Mandatory Conversion), at any time following the earlier of (i) the second anniversary of the closing of the Private Placement or (ii) the occurrence of both of the following: (a) (1) the time that we first administer, after the issue date, a dose of a pharmaceutical product candidate (which such product candidate shall be one of the following candidates, or a variation thereof: DCR-PHXC, DCR-PCSK9 or the undisclosed rare disease program currently in pre-clinical development (each, a Product Candidate)) to a human being pursuant to an IND filed by us with the FDA; or (2) after we have first administered, after the issue date, a dose of a Product Candidate to a human being pursuant to a clinical trial authorization with the Medicine and Healthcare Products Regulatory Agency in the European Union and an IND relating to such Product Candidate has become effective; and (b) we enter into a partnership or license agreement with a major company in the pharmaceutical or biotechnology industry relating to a non-Product Candidate, pursuant to which such company provides us with an up-front cash payment of a minimum amount agreed upon by us and the Lead Investor and agrees to customary future milestone and royalty payments, provided, that, in each case ((i) and (ii)), the trading price of our common stock exceeds 200% of the Conversion Price, as defined below, for 45 out of the 60 most recent trading days. Our ability to require conversion shall be subject to (i) a 19.99% blocker provision to comply with NASDAQ Listing Rules (19.99% Conversion Blocker), (ii) if so elected by an investor, a 9.99% blocker provision (9.99% Conversion Blocker) that will prohibit beneficial ownership of more than 9.99% of the outstanding shares of our common stock or voting power at any time, and (iii) applicable regulatory restrictions. The 19.99% Conversion Blocker and the 9.99% Conversion Blocker are hereinafter referred to as the Conversion Blockers . Conversion Price shall mean an initial price of $3.19 per share, subject to proportionate adjustment for any stock split, stock dividend, combination or other similar recapitalization event.

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

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

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

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

common stock immediately prior to such liquidation, dissolution or winding up.

Upon consummation of a specified change of control transaction, each holder of Redeemable Convertible Preferred will be entitled to receive in preference to the holders of common stock and any junior preferred stock,

Table of Contents

an amount equal to the greater of (i) 101% of the sum of the Accrued Value plus an amount equal to all accrued or declared and unpaid dividends on the Redeemable Convertible Preferred that have not previously been added to the Accrued Value, or (ii) the amount that such shares would have been entitled to receive if they had converted into common stock immediately prior to such event.

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

Upon the effectiveness of the Certificate of Designation, each holder of Redeemable Convertible Preferred will be entitled to receive cumulative dividends on the Accrued Value of each share of Redeemable Convertible Preferred at an initial rate of 12% per annum, compounded quarterly and subject to two rate reductions, of 4% each, upon the occurrence of certain agreed-upon milestone events. Dividends on the Redeemable Convertible Preferred are payable in kind and will accrue on the Accrued Value of each share of Redeemable Convertible Preferred until the earlier of conversion, redemption, consummation of a change of control, a liquidation event, or upon failure to mandatorily convert due to the Conversion Blockers or applicable regulatory restrictions.

In accordance with the terms of the SPA, on March 28, 2017, our board of directors voted to increase the size of the board from eight directors to nine directors and, appointed Adam M. Koppel, M.D., Ph.D., a managing director of the Lead Investor, as a director of our Company, effective immediately following, and contingent upon, the closing of the Private Placement, to fill the resulting vacancy. To the extent such director is not reelected at any time and, so long as the Lead Investor owns at least 25% of the Redeemable Convertible Preferred (or underlying common stock) owned by it at the closing of the Private Placement, it shall have the right to designate a board observer.

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

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

Our GalXC RNAi Technology Platform

The RNAi Therapeutic Modality

All of our GalXC drug discovery and development efforts are based on the therapeutic modality of RNAi, a highly potent and specific mechanism for silencing the activity of a targeted gene. In this naturally occurring

Table of Contents

biological process, double-stranded RNA molecules induce the enzymatic destruction of the mRNA of a target gene that contains sequences that are complementary to one strand of the therapeutic double-stranded RNA molecule. Our approach is to design proprietary double-stranded RNA molecules that have the potential to engage the enzyme Dicer and initiate an RNAi process to silence a specific target gene. We refer to these proprietary molecules generally as DsiRNAs. Our GalXC RNAi platform utilizes a particular Dicer Substrate structure configured for subcutaneous delivery to the liver. Due to the enzymatic nature of RNAi, a single GalXC molecule incorporated into the RNAi machinery can destroy hundreds or thousands of mRNAs from the targeted gene.

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

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

We initiate RNAi through the Dicer enzyme. Our GalXC molecules are structured to be processed by the enzyme Dicer, the initiation point for RNAi in the human cell cytoplasm. Unlike earlier generation RNAi molecules, which mimic the output product of Dicer processing, all our DsiRNAs, including GalXC molecules, enter the RNAi pathway prior to Dicer processing. This can result in preferential use of the correct strand of a double-stranded RNA molecule, and therefore increase the efficacy of the RNAi mechanism. We have found in animal tests that this benefit both increases the potency of our GalXC molecules relative to other RNAi-inducing molecules and enables more sequences to be used compared to other RNAi-inducing molecules. In addition, all our DsiRNAs, including GalXC molecules, have an extended structure relative to conventional RNAi inducing molecules. This extended region presents multiple sites for chemical modification and conjugation compared to earlier RNAi technologies. At these sites, we can use modifications that enhance the drug-like properties on our molecules. Specifically, we can employ modifications that enhance the pharmacokinetic profile and/or suppress immunostimulatory activity.

Our GalXC RNAi platform enables subcutaneous dosing for delivery to the liver. The GalXC RNAi platform is designed to enable convenient subcutaneous delivery for our emerging pipeline of liver-targeted RNAi investigational therapies. The GalXC RNAi platform does not involve LNPs or other formulation components that facilitate drug delivery, which simplifies the platform and eliminates any requirement for functional excipients. Instead, our GalXC molecules are stabilized by chemical modifications and utilize a four base sequence known as a tetraloop, where each base is conjugated to a simple sugar, N-acetylgalactosamine (GalNAc), that is specifically recognized by a receptor on the surface of hepatocyte liver cells. With the GalXC RNAi platform, we believe that a full human dose may be administered via a single subcutaneous injection. After injection, the GalXC molecules enter the bloodstream and are exposed to the liver hepatocytes expressing the GalNAc receptor. After binding to the receptor, the GalXC molecules are internalized by the hepatocyte, ultimately enabling the GalXC molecules to access the RNAi machinery inside the hepatocyte. To date, we have demonstrated *in vivo* gene silencing activity with GalXC molecules after subcutaneous administration against nearly three dozen disease-associated genes in the liver.

11

Table of Contents

Optimization of our GalXC molecules

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

GalXC molecules yield high-potency gene silencing agents. The data are derived from a single GalXC molecule administered subcutaneously at two different dose levels, resulting in potent gene silencing of the target gene in the liver of monkeys. In this example a dose of either 2.0 (red line) or 4.0 (purple line) milligrams per kilogram bodyweight (mg/kg) yields nearly 90% gene silencing after four monthly subcutaneous doses. At 4.0 mg/kg, the full level of gene silencing was still present three months after the last dose.

Our Product Candidates

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

Strength of therapeutic hypothesis. Our current product candidate gene targets, and those we intend to pursue in the future, are a well-understood part of the disease process where a therapeutic intervention is likely to have substantial benefit for the patient.

Readily-identified patient population. We seek disease indications where patients can be readily identified by the presence of characteristic genetic mutations or other readily-accessible disease features. In the case of genetic diseases, these are heritable genetic mutations that can be identified with available genetic tests.

Table of Contents

Predictivity of biomarkers for early efficacy assessment. We seek disease indications where there is a clear relationship between the disease status and an associated biomarker that we can readily measure. This approach will allow us to determine in early stages of clinical development whether our GalXC molecules are likely to have the expected biological and clinical effects in patients.

Unmet medical need. We seek to provide patients with significant benefit and alleviation of disease. The indications we choose to approach have high unmet medical need, which is intended to enable us to better access patients and qualify for pricing and reimbursement that justify our development efforts.

Competitive positioning. We seek indications where we believe we have the opportunity to develop either a first-in-class product or a clearly differentiated therapy.

Rapid development path to approval. To reach commercialization expeditiously and to help ensure our ability to finance development of our product candidates, we have identified indications with the potential for rapid development through marketing approval. Specifically, we believe that some of our product candidates have the potential to obtain breakthrough therapy designation as well as accelerated review process from the FDA.

DCR-PHXC for PH1

In 2016, we announced the first GalXC clinical candidate, DCR-PHXC, which we are developing for the treatment of PH1. PH1 is a rare inborn error of metabolism in which the liver produces excessive levels of oxalate, which in turn causes damage to the kidneys and to other tissues in the body. In preclinical models of PH1, DCR-PHXC reduces oxalate production to near-normal levels, ameliorating the disease condition. DCR-PHXC is in preclinical development, and has advanced into IND-enabling studies. We plan to file an IND and/or CTA for DCR-PHXC in late 2017 and commence human clinical trials in the first quarter of 2018.

PH is a family of rare, inherited autosomal recessive disorders of metabolism in the liver. The most common and severe form of PH is PH1, which usually results in severe damage to the kidneys. 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 production. 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 develop kidney failure (end-stage renal disease, or ESRD) and require transplant. The median age for kidney failure in PH1 patients is 23 years old. While in ESRD, besides having to endure frequent dialysis, patients are afflicted with a build-up of oxalate in the bone, skin, heart, retina, and other tissues with concomitant debilitating complications, a condition known as systemic oxalosis. 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. Currently, aside from dual liver and kidney organ transplantation, there are no highly efficacious therapeutic options for most patients with PH1. Dual liver and kidney transplantation presents a challenge in identifying a donor and is associated with high morbidity and mortality rates. Even in those U.S. patients treated with dual liver and kidney 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 incidence of PH1 is at least one to three per million of population. Based on the frequency of occurrence of disease mutations in the population derived from genome sequence databases, the estimated genetic incidence is six and one half (6.5) per million of population, which we believe suggests that PH1 is under-diagnosed. Roughly consistent with the genetic incidence estimate, 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 Kuwait, have higher incidences due to founder effects or consanguinity. We believe over 1,000

Table of Contents

patients total are currently in 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.

We believe that there is a strong rationale for focusing our RNAi technology on the development of product candidates for the treatment of PH1. The hydroxyproline breakdown metabolic pathway that is disrupted in PH1 consists of a number of enzymes. The gene encoding the final 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 function is disrupted due to mutation, oxalate begins to build up, resulting in progressive loss of kidney function and, ultimately, kidney failure. DCR-PHXC is designed to block the production of oxalate in patients with PH1.

Using DCR-PHXC, and also other GalXC molecules synthesized during the discovery and optimization of DCR-PHXC, we have shown that RNAi can be used to block the production of oxalate in an animal model of PH1. 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. A single dose of DCR-PHXC of 5.0 mg/kg delivered subcutaneously in the animal model of PH1 silences target gene expression by greater than 90% and results in normalization or near normalization of urinary and plasma oxalate levels. We believe these results, if achievable in patients with PH1, would be highly beneficial.

Hypercholesterolemia

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

Hypercholesterolemia is characterized by abnormally high blood serum levels of low-density lipoproteins (LDL) and is one of the key known risk factors for atherosclerosis and cardiovascular disease (CVD). Managing hypercholesterolemia by lowering LDL is one of the cornerstones of the strategy to reduce the risk of CVD morbidity and mortality.

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

Additional programs under investigation involving the liver

In addition to the programs discussed above, the Company has also launched a program targeting a rare disease with high unmet medical need that we believe meets most or all of the key elements of our strategy. We are not disclosing the identity of the disease or gene target at this time. We are investigating a number of diseases associated with genes

expressed in the liver as the basis for potential future programs for development by the Company or potential collaborators. We have selected these target genes and diseases based on our stated

Table of Contents

criteria, including having a strong therapeutic hypothesis, a readily-identifiable patient population, the availability of a potentially predictive biomarker, high unmet medical need, favorable competitive positioning, and what we believe is a rapid projected path to approval. Dicerna has the capacity to launch up to three programs every year, and intends to advance five programs into the clinic by the end of 2019.

Chronic Hepatitis B Virus infection

We are currently using our GalXC RNAi platform to investigate potential pharmaceutical treatments that target HBV. Current therapies rarely lead to a long-term immunological cure as measured by the clearance of HBsAg and sustained HBV DNA suppression. Based on preclinical studies, we believe that our GalXC RNAi platform can produce an experimental HBV-targeted therapy that eliminates HBsAg expression in HBV patients and that has the potential to be delivered in a commercially attractive subcutaneous dosing paradigm.

According to the Hepatitis B Foundation, globally, HBV is reported to be the most common serious liver infection with over 240 million patients chronically infected, according to an estimate by the World Health Organization. Annual mortality directly linked to chronic HBV infection is estimated to be approximately 780,000 people with an estimated 650,000 of these deaths caused by cirrhosis and liver cancer as a result of chronic hepatitis B, and a further 130,000 of these deaths from complications associated with acute disease. Chronic HBV is characterized by the presence of the HBsAg for six months or more.

Nucleoside analogs and pegylated interferon regimens have been utilized to suppress the virus; however neither of them can offer long-term viral suppression for the majority of patients. The vast majority of treated patients do not achieve an immunological cure of chronic HBV infection under treatment with these agents. The chance of achieving a long-term immunological cure as measured by the clearance of HBsAg and sustained HBV DNA suppression may be possible with the introduction of novel drugs designed to reduce intrahepatic and serum HBsAg, as well as HBV DNA.

Intellectual Property

We invest significant amounts in research and development. Our research and development expenses were approximately $41.7 million, $44.0 million and $29.5 million in 2016, 2015 and 2014, respectively.

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

Patents and proprietary rights

We own U.S. patents and a number of pending patent applications with claims to methods and compositions of matter that cover various aspects of our RNAi technology and our discovery technologies, including our proprietary GalXC technology. These U.S. patents include U.S. 8,349,809 (issued in January 2013 with a projected expiration date of January 2030), U.S. 8,513,207 (issued in August 2013 with a projected expiration date of May 2030) and U.S. 8,927,705 (issued in January 2015 with a projected expiration date of July 2030). We also own numerous patents and patent applications covering specific DsiRNA sequences that drive activity against high value disease targets, including KRAS (U.S. 8,372,816; issued in February 2013, with projected expiration in April 2030), HAO1, CTNNB1 (b catenin; U.S. 9,428,752; issued in August 2016, with projected expiration in July 2031), Androgen Receptor (U.S. 8,927,515; issued in January 2015, with projected expiration in September 2031); and

Alpha-1-antitrypsin (U.S. 9,458,457; issued October 4, 2016, with projected expiration in July 2034). Further, we own various applications with claims to methods and compositions of matter related to our lipid delivery technology, such as lipid compositions and particle formulations and the EnCore formulation

Table of Contents

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 future patents issuing from patent applications filed under the research collaboration and license agreement with KHK.

Our strategy around protection of our proprietary technology, including any innovations and improvements, is to obtain patent coverage in various jurisdictions around the world with a focus on jurisdictions that represent significant global pharmaceutical markets. Generally, patents have a term of 20 years from the earliest non-provisional priority date, assuming that all maintenance fees are paid, no portion of the patent has been terminally disclaimed and the patent has not been invalidated. In certain jurisdictions, and in certain circumstances, patent terms can be extended or shortened. We are obtaining worldwide patent protection for at least novel molecules, composition of matter, pharmaceutical formulations, methods of use, including treatment of disease, methods of manufacture and other novel uses for the inventive molecules originating from our research and development efforts. We continuously assess whether it is strategically more favorable to maintain confidentiality for the know-how regarding a novel invention rather than pursue patent protection. For each patent application that is filed we strategically tailor our claims in accordance with the existing patent landscape around a particular technology. There can be no assurance that an issued patent will remain valid and enforceable in a court of law through the entire patent term. Should the validity of a patent be challenged, the legal process associated with defending the patent may be costly and time consuming. Issued patents can be subject to oppositions, interferences, post-grant proceedings, and other third party challenges that can result in the revocation of the patent or limit patent claims such that patent coverage lacks sufficient breadth to protect subject matter that is commercially relevant. Competitors may be able to circumvent our patents. Development and commercialization of pharmaceutical products can be subject to substantial delays and it is possible that at the time of commercialization any patent covering the product will have expired or will be in force for only a short period of time thereafter.

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.

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

It is our policy to require our employees and consultants, outside scientific collaborators, sponsored researchers and other advisors who receive confidential information from us, to execute confidentiality

Table of Contents

agreements upon the commencement of employment or consulting relationships. These agreements provide that all confidential information developed or made known to these individuals during the course of the individual s relationship with us is to be kept confidential and is not to be disclosed to third parties except in specific circumstances. The agreements provide that all inventions conceived by an employee shall be our property. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information.

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

Strategic Partnership

KHK research collaboration and license agreement

In December 2009, we entered into a research collaboration and license agreement with KHK for the research, development and commercialization of drug delivery platforms and DsiRNA molecules for therapeutic targets, primarily in oncology (the collaboration agreement). Under the collaboration agreement, we engaged in the discovery of DsiRNA molecules against KRAS and other gene targets nominated by KHK. Since the initiation of the collaboration agreement, of the various targets in the collaboration, two target programs, including the initial target KRAS, have been nominated by KHK for formal development studies. Both programs utilize our specific RNAi-inducing double-stranded DsiRNA molecules and a lipid nanoparticle drug delivery technology proprietary to KHK. 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 to certain of our technology and patents relating to compounds resulting from the collaboration. KHK has granted us certain non-exclusive licenses in its technology as necessary for us to perform research and development activities as part of the research collaboration.

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 worldwide net sales of products resulting from the research collaboration. The amount of royalty varies depending on the total worldwide 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 KRAS product in the U.S. for an equal share of the profits resulting from U.S. net sales of the product.

If we exercise our option to co-promote a 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 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. In the event we do not exercise our option to co-promote a 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 collaboration agreement at any time upon prior written notice to us until such time as we exercise our option to co-promote under the collaboration agreement. We may terminate the collaboration

Table of Contents

agreement if KHK challenges the validity or enforceability of any patents licensed by us to KHK. Either we or KHK may terminate the collaboration agreement in the event of the bankruptcy or uncured material breach by the other party.

License Agreements

City of Hope license agreement

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

Pursuant to the terms of the license agreement, we paid COH a one-time, non-refundable license fee and issued shares of our common stock to COH and a co-inventor of the core DsiRNA patent. COH is entitled to receive milestone payments in an aggregate amount within the range of $5.0 million to $10.0 million upon achievement of certain clinical and regulatory milestones. COH is further entitled to receive royalties at a low single-digit percentage of any net sale revenue of the licensed products sold by us and our sublicensees. If we sublicense the licensed patent rights to a third party, COH has the right to receive a double digit percentage of sublicense income, the percentage of which decreases after we have expended $12.5 million in development and commercialization costs. We are also obligated to pay COH an annual license maintenance fee of $0.1 million, 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