

Dicerna Pharmaceuticals Inc
Form 424B4
January 30, 2014
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Filed Pursuant to Rule 424(b)(4)
Registration No. 333-193150

PROSPECTUS

6,000,000 Shares

Dicerna Pharmaceuticals, Inc.

Common Stock

We are offering 6,000,000 shares of our common stock. This is our initial public offering and no public market currently exists for our common stock.

Our common stock has been approved for listing on The NASDAQ Global Select Market under the symbol DRNA. We are an emerging growth company as defined by the Jumpstart Our Business Startups Act of 2012 and, as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

Investing in our common stock involves a high degree of risk. Please read Risk Factors beginning on page 10 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	PER SHARE	TOTAL
Public Offering Price	\$ 15.00	\$ 90,000,000
Underwriting Discounts and Commissions ⁽¹⁾	\$ 1.05	\$ 6,300,000
Proceeds to Dicerna Pharmaceuticals, Inc. before expenses	\$ 13.95	\$ 83,700,000

(1) The underwriters will also be reimbursed for certain expenses incurred in this offering. See Underwriting for details. Certain of our existing stockholders, including certain affiliates of our directors, have agreed to purchase an aggregate of 3,400,000 shares of our common stock in this offering at the initial public offering price. The underwriters will receive the same underwriting discount on any shares purchased by these stockholders as they will on any other shares sold to the public in this offering.

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Delivery of the shares of common stock is expected to be made on or about February 4, 2014. We have granted the underwriters an option for a period of 30 days to purchase an additional 900,000 shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be \$7,245,000 and the total proceeds to us, before expenses, will be \$96,255,000.

Joint Book-Running Managers

Jefferies

Leerink Partners

Stifel

Co-Lead Manager

Baird

Prospectus dated January 29, 2014

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We are responsible for the information contained in this prospectus. Neither we nor the underwriters have authorized anyone to provide any information or to make any representations other than those contained in this prospectus or in any free writing prospectuses we have prepared. We do not, and the underwriters do not, take responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus is current only as of its date.

Through and including February 23, 2014 (25 days after the date of this prospectus), all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers obligation to deliver a prospectus when acting as an underwriter and with respect to their unsold allotments or subscriptions.

For investors outside the United States: Neither we nor the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus outside of the United States.

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PROSPECTUS SUMMARY

This summary highlights selected information contained in greater detail elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus carefully, especially the risks of investing in our common stock discussed under Risk Factors and our historical financial statements and related notes included elsewhere in this prospectus, before making an investment decision.

Our Company

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 proprietary RNA interference (RNAi) technology platform, which we believe improves on existing RNAi technologies, to build a broad pipeline in these therapeutic areas. We intend 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 expect to retain substantially all commercial rights in key markets. In oncology and other more prevalent disease areas, we intend to 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.

Our current development programs are as follows.

- n **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. PH1 afflicts an estimated one to three people per million of population and may afflict as many as eight people per million of population and causes severe renal disease and early mortality. 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 intend to begin clinical trials for DCR-PH1 in 2015. We expect to announce initial proof-of-concept clinical data in mid to late 2015.

- n **Other rare inherited diseases involving the liver.** We are investigating a number of other rare diseases involving disease target genes expressed in the liver. These include maple syrup urine disease, familial amyloid polyneuropathy or cardiomyopathy, alpha-1 anti-trypsin hepatocyte inclusions, severe hemophilia A and B and paroxysmal nocturnal hemoglobinuria, among others. In each case, we are seeking to target a clear unmet medical need, a readily-identified patient population, favorable market dynamics, potential orphan drug designation and the possibility to use RNAi-based therapeutics to achieve an optimal combination of high efficacy and low toxicity. Based on the investigation results, we plan to select a specific disease or disorder to further research and develop. We expect to initiate clinical trials in 2015 for any program that we advance into development.

- n **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 and this increased gene expression has been shown to be related to the presence and severity of cancer. 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 and expect to announce initial proof-of-concept clinical data in mid to late 2015. We intend to investigate DCR-M1711 in a variety of tumor types. Our initial focus is on hepatocellular carcinoma (HCC), which we believe represents 85 to 90 percent of primary liver cancer.

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- n **Product candidate for KRAS-related cancers in collaboration with KHK.** 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.

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 in that 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 offers the potential to go beyond traditional therapeutic modalities, such as small molecules and monoclonal antibodies, 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.

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.

- n **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 benefit increases the potency of our DsiRNA molecules relative to other molecules used to induce RNAi.
- n **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 tissue and to solid tumors. Our delivery particles are highly potent, have low toxicity and are amenable to manufacturing in large scale. We have found that, even at doses as low as 13.1µg/kg, we can induce silencing of gene expression at the 50 percent level, which we believe is 100-fold to 1,000-fold 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.
- n **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 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. These agents allow the DsiRNA to be targeted to specific cell types and to enter the cytoplasm of the cell. The targeting agent mediates cell binding and internalization, and the endosomal escape agent mediates 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. RNAi molecules that are not cleaved by Dicer may require the use of cleavable linkers, which are less stable and may be more challenging to synthesize into the RNA strands. We have shown that both conjugation points on our DsiRNAs can be used simultaneously without

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inhibiting processing by the Dicer enzyme. We anticipate that our future product candidates will utilize these conjugation points to improve further the delivery of our DsiRNAs. We are currently developing delivery technologies using this approach to deliver directly our DsiRNAs subcutaneously to liver tissues and ultimately to solid tumors.

The key elements of our strategy are:

- n **Validate our product candidates and our platform in clinical proof-of-concept studies.** Beginning in early 2014, we plan to conduct clinical trials that we believe will generate human proof-of-concept data. We intend to maximize the likelihood of success in those trials by: (1) using genetic analysis 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 our strong data showing the destruction or knockdown of target mRNA molecules induced by double-stranded RNA molecules at preclinical dose levels will translate into clinical results. We expect to initiate clinical trials for DCR-M1711 in the first half of 2014 and for DCR-PH1 in 2015. We expect to announce initial proof-of-concept clinical data for DCR-M1711 and DCR-PH1 in mid to late 2015.
- n **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.
- n **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 key markets. In oncology, we seek to partner our product candidates while retaining meaningful commercial rights in North America.
- n **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 partnerships with pharmaceutical companies across multiple indication areas or in therapeutic areas outside of rare diseases and oncology depending on the attractiveness of the opportunities. These partnerships will provide us with validation of our technology platform, funding to advance our proprietary product candidates and access to development, manufacturing and commercial expertise and capabilities.
- n **Continue to invest in our RNAi technology platform.** We will 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.

Risks related to our business

Our ability to implement our current business strategy is subject to numerous risks, as more fully described in the section titled Risk Factors immediately following this prospectus summary. These risks include, among others, the following.

- n We have no source of predictable revenue, have incurred significant losses since inception, may never become profitable and may incur substantial and increasing net losses for the foreseeable future as we continue development of, and seek regulatory approvals for, our product candidates.
- n Our success is primarily dependent on the successful development, regulatory approval and commercialization of our product candidates, all of which are in early development.

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

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- n If clinical trials of our product candidates fail to demonstrate safety and efficacy, we may be unable to obtain regulatory approvals and commercialize our product candidates.

- n We are subject to regulatory approval processes that are lengthy, time-consuming and unpredictable. We may not obtain approval for any of our product candidates from the U.S. Food and Drug Administration (FDA) or foreign regulatory authorities.

- n Even if we obtain regulatory approval, the market may not be receptive to our product candidates based on a novel therapeutic modality or we may be unable to market any of our product candidates to achieve acceptance and use by the medical community.

- n We may encounter difficulties satisfying the requirements of clinical trial protocols, including patient enrollment.

- n We may never receive milestone payments under our research collaboration and license agreement with KHK or establish and maintain other licenses, collaborations and strategic relationships with terms and timing favorable to us.

- n It is difficult and costly to protect our intellectual property rights.

- n We may face competition from other companies in our field or claims from third parties alleging infringement of their intellectual property.

- n We may be unable to recruit or retain key employees, including our senior management team.

- n We depend on the performance of third parties, including contract research organizations and third-party manufacturers.

- n We will likely need to obtain additional funding on acceptable terms to continue operations.

We are a preclinical stage biopharmaceutical company with a limited operating history. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We do not currently have any product candidates in clinical trials or approved for sale, and we continue to incur significant research and development and general and administrative expenses related to our operations. We are not profitable and have incurred losses in each year since our founding in October 2006. Our net loss for the years ended December 31, 2011 and 2012 was \$8.6 million and \$10.1 million, respectively. Our net loss for the nine months ended September 30, 2013 was \$11.8 million. As of September 30, 2013, we had an accumulated deficit of \$78.7 million. We expect to continue to incur significant losses for the foreseeable future. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods.

Neither we nor our collaborator KHK will be permitted to market our product candidates in the U.S. until we receive regulatory approval from the FDA, and approval by foreign regulatory agencies will be required to market our product candidates in other countries. Neither we nor our collaborator have submitted an application for or received marketing approval for any of our product candidates. Regulatory approval of our product candidates is not guaranteed, and the approval process is expensive and may take several years.

Corporate information

We were incorporated in Delaware in October 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. We maintain a website 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 into, this prospectus and should not be considered part of this prospectus.

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As used in this prospectus, unless otherwise noted, we, us, our and the Company refer to Dicerna Pharmaceuticals, Inc. and, where appropriate, its consolidated subsidiary.

This prospectus and the information incorporated herein by reference include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference in this prospectus are the property of their respective owners.

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Emerging growth company

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 this offering, (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.

As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise generally applicable to public companies. These provisions include:

- n only two years of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced Management's Discussion and Analysis of Financial Condition and Results of Operations disclosure;
- n reduced disclosure about our executive compensation arrangements;
- n no requirement that we hold non-binding advisory votes on executive compensation or golden parachute arrangements; and
- n exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting.

We have taken advantage of some of these reduced burdens, and thus the information we provide stockholders may be different than you might get from other public companies in which you hold shares.

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THE OFFERING

Issuer	Dicerna Pharmaceuticals, Inc.
Shares of common stock offered by us	6,000,000 shares.
Shares of common stock to be outstanding immediately after this offering	16,627,660 shares (17,527,660 if the underwriters exercise in full their option to purchase additional shares of common stock).
Underwriters' option to purchase additional shares of common stock in this offering	We have granted the underwriters a 30-day option to purchase up to 900,000 additional shares at the public offering price less underwriting discounts and commissions.
Dividend policy	We have never paid cash dividends on our common stock and we do not anticipate paying any cash dividends in the foreseeable future. See Dividend Policy.
Use of proceeds	We estimate that the net proceeds from this offering will be approximately \$80.4 million (approximately \$92.9 million if the underwriters exercise in full their option to purchase additional shares of common stock) after deducting the underwriting discounts and commissions and our estimated offering expenses. We expect to use the net proceeds from this offering to fund preclinical and clinical trials of proprietary product candidates, continued technology platform development, working capital and general corporate purposes, as well as potential acquisition or in-licensing activities. See Use of Proceeds.
Proposed NASDAQ symbol	DRNA.
Risk factors	You should carefully read and consider the information set forth under Risk Factors and all other information included in this prospectus for a discussion of factors that you should consider before deciding to invest in shares of our common stock.
Certain of our existing stockholders, including affiliates of our directors, have agreed to purchase an aggregate of 3,400,000 shares of our common stock in this offering at the initial public offering price.	

The number of shares of common stock to be outstanding after this offering excludes, as of December 31, 2013:

- ⁿ 5,950 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2013 under our 2007 Employee, Director and Consultant Stock Plan, as amended;
- ⁿ 1,615,728 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2013 under our 2010 Employee, Director and Consultant Equity Incentive Plan, as amended (2010 Plan);

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- n 115,351 shares of common stock reserved for issuance pursuant to future awards under our 2010 Plan as of December 31, 2013;
- n 1,900,000 shares of common stock reserved for issuance pursuant to future awards under our 2014 Performance Incentive Plan, which will become effective upon the effectiveness of the registration statement to which this prospectus relates;
- n 1,000,000 shares of common stock reserved for issuance pursuant to future awards under our 2014 Employee Stock Purchase Plan, which will become effective upon the effectiveness of the registration statement to which this prospectus relates; and
- n 135,301 shares of common stock issuable upon exercise of warrants outstanding as of December 31, 2013 to purchase shares of common stock, Series A preferred stock, Series B preferred stock or Series C preferred stock, assuming the conversion of all outstanding shares of preferred stock immediately prior to completion of this offering.

Unless otherwise expressly stated or the context otherwise requires, the information in this prospectus accounts for the one-for-250 reverse split of our common stock and the one-for-25 reverse split of our Series A and Series B preferred stock, both of which occurred on July 25, 2013, and assumes or reflects that:

- n the underwriters do not exercise their option to purchase up to 900,000 additional shares of common stock within 30 days from the date of this prospectus;
- n the number of our authorized shares of capital stock has been increased to 150,000,000 shares of common stock and 5,000,000 shares of preferred stock;
- n the amendments to our charter documents and bylaws, which are expected to occur prior to the closing of this offering, have occurred; and
- n the conversion of each share of Series A, Series B and Series C preferred stock into one share of common stock immediately prior to the completion of this offering has occurred.

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The following table sets forth summary financial data for us for the years ended December 31, 2011 and 2012 and for the nine months ended September 30, 2012 and 2013. The summary financial statements of operations data for the fiscal years ended December 31, 2011 and 2012 and the summary balance sheet data as of December 31, 2011 and 2012 are derived from our audited financial statements included elsewhere in this prospectus. The summary financial statements of operations data for the nine months ended September 30, 2012 and 2013 and the summary balance sheet data as of the nine months ended September 30, 2013 are derived from our unaudited condensed financial statements included elsewhere in this prospectus. Our unaudited financial statements are prepared on the same basis as our audited financial statements. We have included, in our opinion, all adjustments, consisting only of normal recurring adjustments, that we consider necessary for a fair presentation of the financial information set forth in those statements. Our historical results are not necessarily indicative of our results to be expected for any future interim financial period, and the results for the nine months ended September 30, 2013 are not necessarily indicative of results to be expected for the full year ending December 31, 2013.

The following summary financial data should be read in conjunction with, and is qualified in its entirety by reference to, Selected Historical Financial Information and Other Data, Management's Discussion and Analysis of Financial Condition and Results of Operations and our historical financial statements and related notes appearing elsewhere in this prospectus.

Summary Financial Data (in thousands except share and per share data)

	YEAR ENDED DECEMBER 31,		NINE MONTHS ENDED SEPTEMBER 30,	
	2011	2012	2012	2013
			<i>(Unaudited)</i>	
Revenue	\$ 7,908	\$ 7,015	\$ 762	\$
Operating expenses:				
Research and development	10,705	11,565	8,078	7,364
General and administrative	4,816	4,700	3,631	3,577
Total operating expenses	15,521	16,265	11,709	10,941
Loss from operations	(7,613)	(9,250)	(10,947)	(10,941)
Other income (expense):				
Preferred stock warrant remeasurement	51	469	352	219
Interest income	3	2	1	1
Loss on extinguishment of debt				(318)
Interest expense	(997)	(1,342)	(1,040)	(760)
Total other income (expense)	(943)	(871)	(687)	(858)
Net loss	\$ (8,556)	\$ (10,121)	\$ (11,634)	\$ (11,799)
Less: Accretion and dividends on redeemable convertible preferred stock	(4,099)	(4,097)	(3,068)	(2,379)
Net loss attributable to common stockholders	\$ (12,655)	\$ (14,218)	\$ (14,702)	\$ (14,178)
Net loss per share attributable to common stockholders Basic and diluted	\$ (492.76)	\$ (516.00)	\$ (533.86)	\$ (505.45)
Weighted average shares outstanding Basic and diluted	25,682	27,554	27,539	28,050
		\$ (4.95)		\$ (2.65)

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Pro forma net loss per share attributable to common stockholders
(unaudited) Basic and diluted

Pro forma weighted average shares outstanding (unaudited) Basic and diluted	2,045,571	4,444,333
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	AS OF SEPTEMBER 30, 2013		
	ACTUAL	PRO FORMA ⁽¹⁾ <i>(Unaudited)</i>	PRO FORMA AS ADJUSTED ⁽²⁾
Balance Sheet Data:			
Cash and cash equivalents	\$ 54,712	\$ 54,712	\$ 135,062
Current assets	55,125	55,125	135,475
Current liabilities	6,560	6,560	6,560
Total assets	56,072	56,072	136,442
Long-term debt net of current portion	1,407	1,407	1,407
Preferred stock warrant liability	436		
Redeemable convertible preferred stock	110,237		
Additional paid-in capital	16,177	126,849	207,199
Accumulated deficit	(78,746)	(78,746)	(78,746)
Total stockholders' equity (deficit)	(62,568)	48,105	128,455

(1) Pro forma balance sheet data give effect to (i) the automatic conversion of all outstanding shares of preferred stock into an aggregate of 10,589,434 shares of common stock upon the closing of this offering and (ii) reclassification of our preferred stock warrants as a component of equity in connection with the conversion of preferred stock warrants into common stock warrants upon the closing of this offering.

(2) Pro forma as adjusted balance sheet data give effect to the automatic conversion of all outstanding shares of preferred stock into an aggregate of 10,589,434 shares of common stock upon the closing of this offering and the sale of 6,000,000 shares of common stock by us in this offering at the initial public offering price of \$15.00 per share, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us and the filing of our amended and restated certificate of incorporation, which will occur immediately prior to the closing of this offering.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the following risk factors and all other information contained in this prospectus before purchasing our common stock. If any of the following risks, as well as other risks and uncertainties occur, our business, financial condition, results of operations and prospects could be materially and adversely affected. In that case, the market price of our common stock could decline and you could lose some or all of your investment.

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 September 30, 2013, we had an accumulated deficit of \$78.7 million. For the twelve months ended December 31, 2011 and 2012 and the nine months ended September 30, 2013, our net loss was \$8.6 million, \$10.1 million and \$11.8 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, KHK has paid us a total of \$17.5 million as of September 30, 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

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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 September 30, 2013, we had \$54.7 million in cash, cash equivalents and short-term investments. Based on our current operating plan, we believe that our available cash, cash equivalents and short-term investments, the net proceeds from this offering and available borrowings under our credit facility, will be sufficient to fund our anticipated level of operations through 2015. 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:

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

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ⁿ 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

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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, public or private 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:

- n variations in the level of expense related to our product candidates or future development programs;
- n 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;
- n the timing of the release of results from any clinical trials conducted by us or our collaborator KHK;
- n 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;
- n any intellectual property infringement lawsuit or opposition, interference or cancellation proceeding in which we may become involved;
- n additions and departures of key personnel;
- n strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- n if any of our product candidates receives regulatory approval, market acceptance and demand for such product candidates;
- n regulatory developments affecting our product candidates or those of our competitors; and
- n 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

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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.

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:

- n the timing of our receipt of any marketing and commercialization approvals;
- n the terms of any approvals and the countries in which approvals are obtained;
- n the safety and efficacy of our product candidates;
- n the prevalence and severity of any adverse side effects associated with our product candidates;
- n limitations or warnings contained in any labeling approved by the FDA or other regulatory authority;
- n relative convenience and ease of administration of our product candidates;
- n the willingness of patients to accept any new methods of administration;
- n the success of our physician education programs;

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

- n the pricing of our products, particularly as compared to alternative treatments; and

- n 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

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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 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:

- n 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;
- n serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- n 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;
- n conditions imposed by the FDA or comparable foreign authorities regarding the scope or design of our clinical trials;
- n delays in enrolling research subjects in clinical trials;

- n high drop-out rates of research subjects;

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

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- n greater than anticipated clinical trial costs;
- n poor effectiveness of our product candidates during clinical trials;
- n unfavorable FDA or other regulatory agency inspection and review of a clinical trial site;
- n 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;
- n 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
- n varying interpretations of data by the FDA and similar foreign regulatory agencies.

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

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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

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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:

- n an inability to initiate or continue clinical trials of product candidates under development;
- n delay in submitting regulatory applications, or receiving regulatory approvals, for product candidates;
- n loss of the cooperation of a collaborator;
- n subjecting our product candidates to additional inspections by regulatory authorities;
- n requirements to cease distribution or to recall batches of our product candidates; and

n 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 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

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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.

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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 Merck & Co., Inc., which has entered into an agreement with Alnylam Pharmaceuticals, Inc. (Alnylam) to sell Sirna Therapeutics, Inc., its wholly owned subsidiary, to Alnylam in a pending transaction announced in January 2014, subject to satisfaction of closing conditions, including the requirements under the Hart-Scott-Rodino Antitrust Improvements Act, and biopharmaceutical companies such as Alnylam, 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 to discover and develop safe and effective means to deliver therapeutic RNAi molecules, such as DsiRNAs, to the relevant cell and tissue types from companies such as Tekmira and Arrowhead.

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 HCC. In addition, Tekmira has announced that it expects to initiate a multicenter, single arm, open label dose escalation Phase 1/2 study for TKM-PLK1 in HCC in the first half of 2014. 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.

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

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

We have limited experience in drug development and 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 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

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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.

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

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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.

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

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

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

We have incurred substantial losses during our history, do not expect to become profitable for the foreseeable future and may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. We may be unable to use these losses to offset income before such unused losses expire. Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an ownership change, which is generally defined as a greater than 50 percentage point change by value in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be further limited. We have not performed an analysis on whether we have experienced any ownership changes in the past. It is possible that we have experienced an ownership change and our net operating losses are subject to such limitation. In addition, additional changes in our stock ownership, including pursuant to this offering, could result in an ownership change. As of December 31, 2012, we had U.S. federal and Massachusetts net operating loss carryforwards of \$47.3 million and \$47.0 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 September 30, 2013, we had \$54.7 million in cash, cash equivalents and fixed income marketable securities. 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. Pending use in our business, we expect to invest the net proceeds of this offering in substantially the same manner. 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 prospectus.

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

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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 December 31, 2013, our patent 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:

- n 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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- n 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.
- n We or our licensors, collaborators or any future collaborators are the first to file patent applications covering certain aspects of our inventions.
- n Others will not independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.
- n A third party may not challenge our patents and, if challenged, a court may not hold that our patents are valid, enforceable and infringed.
- n Any issued patents that we own or have licensed will provide us with any competitive advantages, or will not be challenged by third parties.
- n We may develop additional proprietary technologies that are patentable.
- n The patents of others will not have an adverse effect on our business.
- n 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 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 with respect to such patent rights to manufacture, use, import, offer for sale and sell products covered by

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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

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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.

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

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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 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

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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.

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. (acquired by Merck & Co., Inc. in 2006), 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 January 2014, Alnylam announced that it had entered into an agreement to acquire Sirna Therapeutics, subject to satisfaction of closing conditions, including the requirements under the Hart-Scott-Rodino Antitrust Improvements Act. If Alnylam completes its acquisition of Sirna Therapeutics or assets related to Sirna Therapeutics' RNAi intellectual property, we expect that the appeal would likely 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 is upheld on appeal and 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

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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 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

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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.

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 or any

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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 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:

- n 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;
- n 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;
- n 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;
- n 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

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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.

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If our operations are found to be in violation of any such requirements, we may be subject to penalties, including civil or criminal penalties, monetary damages, the curtailment or restructuring of our operations, loss of eligibility to obtain approvals from the FDA, or exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, any of which could adversely affect our financial results. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time and resources.

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:

- n adverse regulatory inspection findings;
- n warning letters;
- n voluntary or mandatory product recalls or public notification or medical product safety alerts to healthcare professionals;
- n restrictions on, or prohibitions against, marketing our products;
- n restrictions on, or prohibitions against, importation or exportation of our products;
- n suspension of review or refusal to approve pending applications or supplements to approved applications;
- n exclusion from participation in government-funded healthcare programs;
- n exclusion from eligibility for the award of government contracts for our products;
- n suspension or withdrawal of product approvals;
- n product seizures;
- n injunctions; and
- n 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.

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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.

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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:

- n they are incident to a physician's services;
- n 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
- n they have been approved by the FDA and meet other requirements of the statute.

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.

- n 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.
- n 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.
- n 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.

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- 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.

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- n 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.

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:

- n regulatory authorities may withdraw their approval of the product or seize the product;
- n we may be required to recall the product or change the way the product is administered to patients;
- n additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof;
- n we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- n regulatory authorities may require the addition of labeling statements, such as a black box warning or a contraindication;

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- n we may be required to create a Medication Guide outlining the risks of such side effects for distribution to patients;
- n we could be sued and held liable for harm caused to patients;
- n the product may become less competitive; and
- n our reputation may suffer.

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Risks Related to Our Common Stock and This Offering

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 this prospectus and 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. In addition, as an emerging growth company, we are only required to provide two years of audited financial statements and two years of selected financial data in this prospectus. 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 this prospectus and 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 likely to be volatile. As a result of this volatility, investors may not be able to sell their common stock at or above the initial public offering price. The market price for our common stock may be influenced by many factors, including the other risks described in this section of the prospectus titled **Risk Factors** and the following:

- n the success of competitive products or technologies;
- n results of preclinical and clinical studies of our product candidates, or those of our competitors, our existing collaborator or any future collaborators;
- n regulatory or legal developments in the U.S. and other countries, especially changes in laws or regulations applicable to our products;
- n introductions and announcements of new products by us, our commercialization partners, or our competitors, and the timing of these introductions or announcements;
- n actions taken by regulatory agencies with respect to our products, clinical studies, manufacturing process or sales and marketing terms;

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- n actual or anticipated variations in our financial results or those of companies that are perceived to be similar to us;
- n the success of our efforts to acquire or in-license additional technologies, products or product candidates;
- n developments concerning our collaborations, including but not limited to those with our sources of manufacturing supply and our commercialization partners;
- n announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;

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- n developments or disputes concerning patents or other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our products;
- n our ability or inability to raise additional capital and the terms on which we raise it;
- n the recruitment or departure of key personnel;
- n changes in the structure of healthcare payment systems;
- n market conditions in the pharmaceutical and biotechnology sectors;
- n 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;
- n our failure or the failure of our competitors to meet analysts projections or guidance that we or our competitors may give to the market;
- n fluctuations in the valuation of companies perceived by investors to be comparable to us;
- n announcement and expectation of additional financing efforts;
- n speculation in the press or investment community;
- n trading volume of our common stock;
- n sales of our common stock by us or our stockholders;
- n the absence of lock-up agreements in connection with this offering with the holders of substantially all of our outstanding shares;
- n the concentrated ownership of our common stock;
- n changes in accounting principles;
- n terrorist acts, acts of war or periods of widespread civil unrest;

n natural disasters and other calamities; and

n 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.

You will experience immediate and substantial dilution as a result of this offering and may experience additional dilution in the future.

If you purchase common stock in this offering, you will incur immediate and substantial dilution of \$7.27 per share, representing the difference between the initial public offering price of \$15.00 per share and our pro forma net tangible book value per share as of September 30, 2013 after giving effect to this offering and the conversion of all outstanding shares of our preferred stock upon the closing of this offering. Moreover, we issued warrants and options in the past to acquire common stock at prices significantly below the initial public offering price. As of December 31, 2013, there were 135,301 shares subject to outstanding warrants and 1,621,678 shares subject to outstanding options. To the extent that these outstanding warrants or options are ultimately exercised, you will incur further dilution.

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.

Substantially all of our outstanding shares will not be subject to lock-up agreements in connection with this offering. 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 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

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them for a period of 180 days following the date of this prospectus. 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 this offering have not entered into any lock-up agreements in connection with this offering. As a result, a substantial number of shares of our common stock will be available for sale in the public market after the completion of this offering. The sale of a significant number of shares of our common 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, if a significant number of shares of our common stock were to be sold immediately after the completion of this offering, this would decrease the likelihood that the underwriters would exercise all or part of their over-allotment option and, consequently, decrease the likelihood that we will receive the additional net proceeds from such an exercise.

Based on shares of our capital stock outstanding as of December 31, 2013 and assuming the underwriters do not exercise their option to purchase up to 900,000 additional shares of common stock, we will have 16,627,660 shares of common stock outstanding after the completion of this offering, including the 6,000,000 shares of common stock that we are selling in this offering which may be resold in the public market immediately. Based on 10,627,660 shares of common stock outstanding as of December 31, 2013 assuming the conversion of our preferred stock, the shares of our common stock (excluding the shares sold in this offering) that will be available for sale in the public market, subject to any applicable volume limitations under federal securities laws with respect to affiliate sales, either immediately after the completion of this offering or in the near future are as follows:

- n beginning on the date of this prospectus, approximately 701,085 shares of our common stock, or 6.6 percent of such total outstanding shares of our common stock as of December 31, 2013, will be immediately available for sale in the public market;
- n beginning 90 days after the date of this prospectus, an additional approximately 9,913,442 shares of our common stock, or 93.3 percent of such total outstanding shares of our common stock as of December 31, 2013, will be eligible for sale in the public market from time to time thereafter, subject in some cases to the volume and other restrictions of Rule 144 of the Securities Act of 1933, as amended; and
- n beginning 180 days after the date of this prospectus, the remainder of the shares of our common stock will be eligible for sale in the public market due to the expiration of the lock-up agreements between our executive officers and the underwriters, unless the representatives of the underwriters waive the provisions of these lock-up agreements and allow these stockholders to sell their shares earlier.

In addition, as of December 31, 2013, there were 135,301 shares subject to outstanding warrants, 1,621,678 shares subject to outstanding options and an additional 115,351 shares reserved for future issuance under our employee benefit plans that will become eligible for sale in the public market to the extent permitted by any applicable vesting requirements, the lock-up agreements and Rules 144 and 701 under the Securities Act of 1933, as amended.

Moreover, immediately after this offering, holders of an aggregate of up to 10,593,858 shares of our common stock and holders of warrants to purchase 135,301 shares of our common stock will 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. We also intend to register all shares of common stock that we may issue under our equity incentive plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates under Rule 144 and the lock-up agreements. For more information, see [Shares Eligible for Future Sale](#).

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.

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An active trading market for our common stock may not develop.

Prior to this offering, there has been no public market for our common stock. The initial public offering price for our common stock was determined through negotiations with the underwriters. Although our common stock has been approved for listing on The NASDAQ Global Select Market, an active trading market for our shares may never develop or be sustained following this offering. If an active market for our common stock does not develop, it may be difficult for you to sell shares you purchase in this offering without depressing the market price for the shares or at all.

Because our management will have broad discretion over the use of the net proceeds from this offering, you may not agree with how we use them and the proceeds may not be invested successfully.

We intend to use the net proceeds to us from this offering to fund research and development and clinical trial expenses and potential in-licensing of intellectual property and technology, and other general corporate purposes, including funding the costs of operating as a public company, and therefore, our management will have broad discretion as to the use of the offering proceeds. Accordingly, you will be relying on the judgment of our management with regard to the use of these net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. It is possible that the proceeds will be invested in a way that does not yield a favorable, or any, return for our company.

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. We do not currently have and may never obtain research coverage by securities and industry analysts. If no or few securities or industry analysts commence coverage of us, the trading price for our stock would be negatively impacted. In the event we obtain securities or industry analyst coverage, if any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our target studies and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

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

Based on the beneficial ownership of our common stock as of December 31, 2013, after this offering, our executive officers and directors, together with holders of five percent or more of our outstanding common stock before this offering and their respective affiliates, will beneficially own approximately 37.1 percent of our outstanding common stock (assuming no exercise of the underwriters' option to purchase additional shares of common stock). After giving effect to purchases by certain of our existing stockholders, including certain affiliates of our directors, in this offering, our directors, executive officers and principal stockholders, together with their affiliates, will beneficially own, in the aggregate, approximately 57.5 percent of our outstanding common stock, or 54.6 percent of our outstanding common stock if the underwriters exercise their overallotment option in full, upon the completion of this offering, based on shares of our capital stock outstanding as of December 31, 2013. 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 your interests. 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

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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:

- n a prohibition on actions by our stockholders by written consent;

- n 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);

- n advance notice requirements for election to our board of directors and for proposing matters that can be acted upon at stockholder meetings; and

- n the authority of the board of directors to issue preferred stock with such terms as the board of directors may determine.

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

We 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

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identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. In addition, if we are not able to continue to meet these requirements, we may not be able to remain listed on The NASDAQ Global Select Market.

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

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, our loan and security agreement with Hercules Technology II, L.P. 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 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.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements that involve risks and uncertainties. All statements other than statements of historical facts contained in this prospectus are forward-looking statements. 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, ongoing or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- n 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;
- n 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;
- n 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;
- n our ability to identify and develop product candidates for treatment of additional disease indications;
- n our or a collaborator's ability to obtain and maintain regulatory approval of any of our product candidates;
- n the rate and degree of market acceptance of any approved products candidates;
- n the commercialization of any approved product candidates;
- n our ability to establish and maintain additional collaborations and retain commercial rights for our product candidates in the collaborations;
- n the implementation of our business model and strategic plans for our business, technologies and product candidates;
- n our estimates of our expenses, ongoing losses, future revenue and capital requirements;
- n our ability to obtain additional funds for our operations;
- n 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;
- n our reliance on third parties to conduct our preclinical studies or any future clinical trials;

- n 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;
- n our ability to attract and retain qualified key management and technical personnel;
- n our use of net proceeds to us from this offering;
- n our expectations regarding the time during which we will be an emerging growth company under the Jumpstart Our Business Startups Act;
- n our financial performance; and
- n developments relating to our competitors or our industry.

These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those described in the section titled **Risk Factors** and elsewhere in this prospectus.

Any forward-looking statement in this prospectus 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.

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This prospectus 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.

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STATISTICAL DATA AND MARKET INFORMATION

This prospectus contains estimates, projections and other statistical data made by independent parties and by us relating to market size and growth, the incidence of certain medical conditions and other industry data. These data, to the extent they contain estimates or projections, involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates or projections. Industry publications and other reports we have obtained from independent parties generally state that the data contained in these publications or other reports have been obtained in good faith or from sources considered to be reliable, but they do not guarantee the accuracy or completeness of such data. The industry in which we operate is subject to risks and uncertainties due to a variety of factors, including those described in the Risk Factors section of this prospectus. These and other factors could cause results to differ materially from those expressed in these publications and reports.

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USE OF PROCEEDS

We estimate that our net proceeds from the sale of the shares of common stock will be approximately \$80.4 million, at the initial public offering price of \$15.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that we will receive net proceeds from this offering of approximately \$92.9 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering as follows:

- n approximately \$16.0 million for additional preclinical studies and Phase 1 clinical trials for DCR-M1711 to evaluate safety and biological markers of efficacy in oncology patients;
- n approximately \$10.0 million for preclinical studies and Phase 1 clinical trials of DCR-PH1 to evaluate safety and biological markers of efficacy in patients with Primary Hyperoxaluria 1; and
- n approximately \$10.0 million for preclinical studies and clinical trials of another liver target that we plan to identify and advance into development in 2015.

We intend to use the remainder of the net proceeds from this offering for continued technology platform development, working capital and general corporate purposes. Although we may use a portion of the net proceeds of this offering for the acquisition or licensing of product candidates, technologies, intellectual property, other assets or complementary businesses, we have no current understandings, agreements or commitments to do so.

The expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures depend on numerous factors, including the progress of our preclinical development efforts, the results of any clinical trials and other studies and any unforeseen cash needs. All of our research and development programs are at an early stage and successful development of 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 product candidate and are difficult to predict. As a result, we cannot currently specify in more detail the percentage of the net proceeds that we may use for each of the listed purposes. Accordingly, we will have broad discretion in the use of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our stock.

Pending the use of the proceeds from this offering, we intend to invest the net proceeds in short-term, interest-bearing, investment-grade securities, certificates of deposit or government securities.

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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.

Table of Contents**CAPITALIZATION**

The following table sets forth our cash and cash equivalents and capitalization as of September 30, 2013:

- n on an actual basis;
- n on a pro forma basis to reflect the conversion of all of our outstanding preferred stock into common stock, which will occur automatically immediately prior to completion of this offering; and
- n on a pro forma as adjusted basis to reflect the conversion referred to above and the sale of 6,000,000 shares of common stock by us in this offering at the initial public offering price of \$15.00 per share, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us and the filing of our amended and restated certificate of incorporation, which will occur immediately prior to the closing of this offering.

You should read this table in conjunction with our financial statements and related notes and the sections titled "Selected Historical Financial Information and Other Data," "Management's Discussion and Analysis of Financial Condition and Results of Operations," "Use of Proceeds" and "Description of Capital Stock" appearing elsewhere in this prospectus.

	AS OF SEPTEMBER 30, 2013		
	ACTUAL	PRO FORMA	PRO FORMA AS ADJUSTED
Cash and cash equivalents	\$ 54,712	\$ 54,712	\$ 135,062
Long-term debt net of current portion	\$ 1,407	\$ 1,407	\$ 1,407
Preferred stock warrant liability	436		
Redeemable convertible preferred stock, \$0.0001 par value per share:			
Series A: 880,000 shares designated, 855,996 shares issued and outstanding, actual; no shares designated, issued or outstanding, pro forma and pro forma as adjusted	21,400		
Series B: 1,190,000 shares designated, 1,162,021 shares issued and outstanding, actual; no shares designated, issued or outstanding, pro forma and pro forma as adjusted	29,050		
Series C: 9,000,000 designated, 8,571,417 issued and outstanding, actual; no shares designated, issued or outstanding, pro forma and pro forma as adjusted	59,787		
Total redeemable convertible preferred stock	110,237		
Stockholders' equity (deficit):			
Common stock, \$0.0001 par value per share; authorized 15,000,000 shares, 28,093 shares issued and outstanding, actual; authorized 15,000,000 shares, 10,617,527 shares issued and outstanding, pro forma; authorized 150,000,000 shares, 16,617,527 shares issued and outstanding, pro forma as adjusted	1	2	2
Additional paid-in capital	16,177	126,849	207,199
Accumulated deficit	(78,746)	(78,746)	(78,746)
Total stockholders' equity (deficit)	(62,568)	48,105	128,455
Total capitalization	\$ 49,512	\$ 49,512	\$ 129,862

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The number of shares of common stock issued and outstanding actual, pro forma and pro forma as adjusted in the table above excludes the following shares as of September 30, 2013 (giving effect to the reverse stock split effected by us on July 25, 2013):

- n 11,187 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2013 under our 2007 Employee, Director and Consultant Stock Plan, as amended, at a weighted average exercise price of \$3.42 per share;
- n 1,415,020 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2013 under our 2010 Employee, Director and Consultant Equity Incentive Plan, as amended (2010 Plan), at a weighted average exercise price of \$3.42 per share;
- n 320,955 shares of common stock reserved for issuance pursuant to future awards under the 2010 Plan as of September 30, 2013;
- n 1,900,000 shares of common stock reserved for issuance pursuant to future awards under our 2014 Performance Incentive Plan, which will become effective upon the effectiveness of the registration statement to which this prospectus relates;
- n 1,000,000 shares of common stock reserved for issuance pursuant to future awards under our 2014 Employee Stock Purchase Plan, which will become effective upon the effectiveness of the registration statement to which this prospectus relates; and
- n 135,301 shares of common stock issuable upon exercise of warrants outstanding as of September 30, 2013 to purchase shares of common stock, Series A preferred stock, Series B preferred stock or Series C preferred stock, assuming the conversion of all outstanding shares of preferred stock immediately prior to the completion of this offering, at a weighted average exercise price of \$17.25 per share.

Table of Contents**DILUTION**

If you invest in our common stock, your interest will be diluted to the extent of the difference between the public offering price per share of our common stock that you pay and the pro forma as adjusted net tangible book value per share of our common stock after this offering. Net tangible book value per share is determined by dividing our total tangible assets less our total liabilities by the number of shares of common stock outstanding. Our historical net tangible book value as of September 30, 2013 was \$47.7 million, or \$1,696.83 per share, based on 28,093 shares of common stock outstanding as of September 30, 2013. Our pro forma net tangible book value as of September 30, 2013 was \$48.1 million, or \$4.53 per share, based on the total number of shares of our common stock outstanding as of September 30, 2013, after giving effect to the automatic conversion of all outstanding shares of our preferred stock as of September 30, 2013 into an aggregate of 10,589,434 shares of common stock immediately prior to the completion of this offering.

Net tangible book value dilution per share represents the difference between the amount per share paid by new investors who purchase shares from us in this offering and the pro forma net tangible book value per share of common stock immediately after completion of this offering. As of September 30, 2013, after giving effect to our sale of 6,000,000 shares of common stock in this offering at the initial offering price of \$15.00 per share, and after deducting estimated underwriting discounts and commissions and estimated offering expenses that we must pay, our pro forma as adjusted net tangible book value would have been \$128.4 million, or \$7.73 per share. This represents an immediate increase in pro forma net tangible book value of \$3.20 per share to existing stockholders, and an immediate dilution in pro forma net tangible book value of \$7.27 per share to new investors purchasing shares in this offering. The table below illustrates this per share dilution as of September 30, 2013.

Initial public offering price per share		\$ 15.00
Historical net tangible book value per share as of September 30, 2013	\$ 1,696.83	
Decrease in pro forma net tangible book value per share as of September 30, 2013 attributable to the conversion of preferred stock	\$ (1,692.30)	
Pro forma net tangible book value per share as of September 30, 2013, before giving effect to this offering	\$ 4.53	
Increase in pro forma net tangible book value per share attributable to new investors participating in this offering	\$ 3.20	
Pro forma as adjusted net tangible book value per share after this offering		\$ 7.73
Dilution of pro forma net tangible book value per share to new investors		\$ 7.27

If the underwriters exercise their option to purchase additional shares in full, our pro forma as adjusted net tangible book value will increase to \$8.05 per share, representing an increase to existing holders of \$3.52 per share, and there will be an immediate dilution of \$6.95 per share to new investors.

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The following table sets forth, on a pro forma as adjusted basis as of September 30, 2013, the number of shares of common stock purchased or to be purchased from us, the total consideration paid or to be paid and the average price per share paid or to be paid by existing holders of common stock and by new investors, at the initial public offering price of \$15.00 per share, before deducting estimated underwriting discounts and commissions and estimated offering expenses that we must pay.

	SHARES PURCHASED		TOTAL CONSIDERATION		AVERAGE PRICE
	NUMBER	PERCENT	AMOUNT	PERCENT	PER SHARE
Existing stockholders	10,617,527	63.9%	\$ 110,756,489	55.2%	\$ 10.43
New investors	6,000,000	36.1%	\$ 90,000,000	44.8%	\$ 15.00
Total	16,617,527	100.0%	\$ 200,756,489	100.0%	\$ 12.08

The foregoing discussion and tables are based on the number of shares of common stock outstanding as of September 30, 2013 (taking into account the conversion of our preferred stock outstanding as of September 30, 2013, which will occur automatically upon the completion of this offering), and exclude:

- n 11,187 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2013 under our 2007 Employee, Director and Consultant Stock Plan, as amended, at a weighted average exercise price of \$3.42 per share;
- n 1,415,020 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2013 under our 2010 Employee, Director and Consultant Equity Incentive Plan, as amended (2010 Plan), at a weighted average exercise price of \$3.42 per share;
- n 320,955 shares of common stock reserved for issuance pursuant to future awards under the 2010 Plan as of September 30, 2013;
- n 1,900,000 shares of common stock reserved for issuance pursuant to future awards under our 2014 Performance Incentive Plan, which will become effective upon the effectiveness of the registration statement to which this prospectus relates;
- n 1,000,000 shares of common stock reserved for issuance pursuant to future awards under our 2014 Employee Stock Purchase Plan, which will become effective upon the effectiveness of the registration statement to which this prospectus relates; and
- n 135,301 shares of common stock issuable upon exercise of warrants outstanding as of September 30, 2013 to purchase shares of common stock, Series A preferred stock, Series B preferred stock or Series C preferred stock, assuming the conversion of all outstanding shares of preferred stock immediately prior to the completion of this offering, at a weighted average exercise price of \$17.25 per share.

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If the underwriters exercise their option to purchase additional shares of our common stock in full, our existing stockholders would own 60.6 percent and our new investors would own 39.4 percent of the total number of shares of our common stock outstanding upon completion of this offering. The total consideration paid by our existing stockholders would be approximately \$110.8 million, or 51.7 percent, and the total consideration paid by our new investors would be \$103.5 million, or 48.3 percent.

Certain of our existing stockholders, including certain affiliates of our directors, have agreed to purchase an aggregate of 3,400,000 shares of our common stock in this offering at the initial public offering price. For dilution purposes, the shares purchased and consideration paid by those stockholders in this offering at the initial public offering price set forth in the foregoing discussion and tables are reflected as shares purchased and consideration paid by new investors.

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The following table sets forth selected financial data for us for the years ended December 31, 2011 and December 31, 2012, and the nine months ended September 30, 2012 and 2013. The selected financial data for the fiscal years ended December 31, 2011 and 2012 were derived from our audited financial statements included elsewhere in this prospectus. Our selected financial data for the nine months ended September 30, 2012 and 2013 were derived from our unaudited condensed financial statements included elsewhere in this prospectus. The unaudited financial statements reflect, in the opinion of management, all adjustments necessary for the fair presentation of the financial condition and the results of operations for such periods. Operating results for the nine months ended September 30, 2013 are not necessarily indicative of the results that may be expected for the entire year ending December 31, 2013.

The financial data set forth below should be read in conjunction with, and are qualified in their entirety by, reference to Management's Discussion and Analysis of Financial Condition and Results of Operations, and our historical financial statements and related notes included elsewhere in this prospectus.

Selected Financial Data (in thousands except share and per share data)

	YEAR ENDED DECEMBER 31,		NINE MONTHS ENDED SEPTEMBER 30,	
	2011	2012	2012 <i>(Unaudited)</i>	2013
Revenue	\$ 7,908	\$ 7,015	\$ 762	\$
Operating expenses:				
Research and development	10,705	11,565	8,078	7,364
General and administrative	4,816	4,700	3,631	3,577
Total operating expenses	15,521	16,265	11,709	10,941
Loss from operations	(7,613)	(9,250)	(10,947)	(10,941)
Other income (expense):				
Preferred stock warrant remeasurement	51	469	352	219
Interest income	3	2	1	1
Loss on extinguishment of debt				(318)
Interest expense	(997)	(1,342)	(1,040)	(760)
Total other income (expense)	(943)	(871)	(687)	(858)
Net loss	\$ (8,556)	\$ (10,121)	\$ (11,634)	\$ (11,799)
Loss: Accretion and dividends on redeemable convertible preferred stock	(4,099)	(4,097)	(3,068)	(2,379)
Net loss attributable to common stockholders	\$ (12,655)	\$ (14,218)	\$ (14,702)	\$ (14,178)
Net loss per share attributable to common stockholders - Basic and diluted	\$ (492.76)	\$ (516.00)	\$ (533.86)	\$ (505.45)
Weighted average shares outstanding - Basic and diluted	25,682	27,554	27,539	28,050
		\$ (4.95)		\$ (2.65)

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Pro forma net loss per share attributable to common stockholders
(unaudited) Basic and diluted

Pro forma weighted average shares outstanding (unaudited) Basic and diluted	2,045,571	4,444,333
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	AS OF DECEMBER 31,		AS OF SEPTEMBER
	2011	2012	30, 2013 <i>(Unaudited)</i>
Balance Sheet Data:			
Cash and cash equivalents	\$ 22,490	\$ 3,670	\$ 54,712
Current assets	23,023	9,032	55,125
Current liabilities	5,299	5,671	6,560
Total assets	24,637	10,191	56,072
Long-term debt net of current portion	8,735	4,660	1,407
Preferred stock warrant liability	800	331	436
Redeemable convertible preferred stock	60,151	64,248	110,237
Common stock	1	1	1
Additional paid-in capital			16,177
Accumulated deficit	(50,634)	(64,720)	(78,746)
Total stockholders' deficit	(50,633)	(64,719)	(62,568)

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MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes thereto included elsewhere in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the Risk Factors section of this prospectus, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

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 intend 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 expect to retain substantially all commercial rights in key markets. In oncology and other more prevalent disease areas, we intend to 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 intend 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 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 an 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 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 Technology II, L.P. (Hercules loan) to fund our operations. More particularly, since our inception and through September 30, 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 (Series C bridge loan)), \$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 September 30, 2013, our cash and cash equivalents were

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\$54.7 million and we also had \$0.3 million in restricted cash. In addition, in July 2013, we issued 8,142,891 shares of Series C preferred stock for \$57.0 million in gross proceeds and issued 428,526 shares of Series C preferred stock in satisfaction of the \$3.0 million Series C bridge loan.

Since inception, we have incurred significant operating losses. Our net loss was \$8.6 million and \$10.1 million for the years ended December 31, 2011 and 2012, respectively, and \$11.6 million and \$11.8 million for the nine months ended September 30, 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 \$0.8 million for the nine months ended September 30, 2012. No revenue was recognized for the nine months ended September 30, 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 September 30, 2013, we had an accumulated deficit of \$78.7 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:

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

Collaboration agreement

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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

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studies. Both programs utilize our specific RNAi-inducing double-stranded DsiRNA molecules and a lipid nanoparticle drug delivery technology proprietary to KHK. As of September 30, 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 for accounting purposes.

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

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

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 have not received any royalty payments as of September 30, 2013.

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The following table summarizes the sources of our revenue for the years ended December 31, 2011 and 2012 and the nine months ended September 30, 2013 (in thousands).

	YEAR ENDED		NINE MONTHS
	DECEMBER 31, 2011	DECEMBER 31, 2012	ENDED SEPTEMBER 30, 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:

- n 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;
- n platform-related lab expenses, including lab supplies, license fees and costs of consultants;
- n employee-related expenses, including salaries, benefits and stock-based compensation expense; and
- n facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation of leasehold improvements and equipment and laboratory and other supplies.

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

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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 and 2012 and the nine months ended September 30, 2013 (in thousands).

	YEAR ENDED		NINE MONTHS
	DECEMBER 31, 2011	DECEMBER 31, 2012	ENDED SEPTEMBER 30, 2013
Direct research and development expenses	\$ 312	\$ 1,315	\$ 2,837
Platform-related expenses	5,948	5,931	1,806
Employee-related expenses	3,445	3,264	1,943
Facilities, depreciation and other expenses	1,000	1,055	778
Total	\$ 10,705	\$ 11,565	\$ 7,364

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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 and 2012 and the nine months ended September 30, 2013 (in thousands).

	YEAR ENDED		NINE MONTHS
	DECEMBER 31, 2011	DECEMBER 31, 2012	ENDED SEPTEMBER 30, 2013
General and administrative expenses	\$ 4,816	\$ 4,700	\$ 3,577

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 Series C bridge loan, and the Hercules loan.

Preferred stock warrant remeasurement

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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).

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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 financial statements, which have been prepared in accordance with accounting principles general accepted in the U.S. (GAAP). The preparation of these 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 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 financial statements appearing in this prospectus, 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 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.

Table of Contents***Preferred stock warrants liability***

As of September 30, 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 this offering will result in the conversion of all classes of our preferred stock into common stock. Upon such conversion of the underlying classes of preferred stock, the remaining warrants to purchase Series A, Series B and Series C preferred stock will be classified as a component of equity and no longer be 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 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, 2012, the federal and state net operating loss carryforwards were approximately \$47.3 million and \$47.0 million, respectively, and the federal and state research and development carryforwards were \$0.7 million and \$0.6 million, respectively. These tax credits begin to expire in 2028. At December 31, 2012, we had \$0.6 million of unrecognized tax benefits, of which \$0.6 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 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 will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available. 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.

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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.

We have computed the fair value of employee stock options at date of grant using the following assumptions.

	YEAR ENDED DECEMBER 31,	
	2011	2012
Expected volatility	58%	64%
Expected term (in years)	6.00	6.00
Risk-free interest rate	0.9%	0.7%
Expected dividend yield	%	%

The assumptions used to estimate fair value for nonemployee stock options were as follows: (1) risk-free interest rate of 2.0 percent, 1.7 percent and 2.8 percent as of December 31, 2011 and 2012 and September 30, 2013, respectively, (2) expected volatility of 58 percent, 64 percent and 66 percent as of December 31, 2011 and 2012 and as of September 30, 2013, respectively, (3) remaining life of approximately seven years and (4) no expected dividends for the years ended December 31, 2011 and 2012 and the nine months ended September 30, 2013.

Stock-based compensation for employees and non-employees were allocated as outlined below (in thousands).

	YEAR ENDED DECEMBER 31,		NINE MONTHS ENDED SEPTEMBER 30,	
	2011	2012	2012	2013
Research and development	\$ 52	\$ 14	\$ 13	\$ 33
General and administrative	121	111	81	120
Total	\$ 173	\$ 125	\$ 94	\$ 153

As of September 30, 2013, we had \$2.6 million of total unrecognized compensation expense, net of related forfeiture estimates, which is expected to be recognized over a weighted-average remaining vesting period of approximately 22 months. We expect the impact of our stock-based compensation expense for stock options and restricted stock granted to employees and non-employees to grow in future periods due to the potential increases in the value of our common stock and headcount.

Stock option grants

The dates of our contemporaneous valuations have not always coincided with the dates of our stock-based compensation grants. In determining the exercise prices of the options set forth in the table below, our board of directors considered, among other things, the most recent contemporaneous valuations of our common stock and our assessment of additional objective and subjective factors we believed were relevant as of the grant date. The additional factors considered when determining any changes in fair value between the most recent contemporaneous valuation and the grant dates included, when available, the prices paid in recent transactions involving our equity securities, as well as our stage of development, our operating and financial performance and current business conditions.

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The following table summarizes stock options granted from January 1, 2012 through the date of this prospectus.

GRANT DATE	AWARD TYPE	NUMBER OF COMMON SHARES UNDERLYING OPTIONS GRANTED	EXERCISE PRICE (OPTIONS) OR PURCHASE PRICE (RESTRICTED STOCK) PER SHARE	COMMON STOCK FAIR VALUE PER SHARE ON GRANT DATE
April 27, 2012	Option	3,330	\$ 50.00	\$ 50.00
September 11, 2012	Option	50	\$ 50.00	\$ 50.00
September 24, 2013	Option	1,401,000	\$ 3.42	\$ 3.42
December 4, 2013	Option	49,750	\$ 3.42	\$ 7.42 ⁽¹⁾
December 30, 2013	Option	156,250	\$ 3.42	\$ 7.42 ⁽¹⁾

⁽¹⁾ At the time of the option grants on December 4, 2013 and December 30, 2013, our board of directors determined that the fair value of our 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 as of each of the grant dates. However, as described below, a preliminary retrospective valuation, which was completed in early January 2014 and reasonably assumed the successful closing of this offering in the near term with the then estimated price range of \$11.00 to 13.00, estimated the fair value of our common stock was \$7.42 as of December 31, 2013.

Based on the initial public offering price of \$15.00 per share, the aggregate intrinsic value of the stock options granted on September 24, 2013 and outstanding as of September 30, 2013 was \$16.2 million, of which \$0.7 million and \$15.5 million related to the stock options that were vested and unvested, respectively, at that date. Based on the initial public offering price of \$15.00 per share, the aggregate intrinsic value of the stock options granted on September 24, December 4 and December 30, 2013 and outstanding as of December 31, 2013 was \$18.6 million, of which \$1.5 million and \$17.1 million related to stock options that were vested and unvested, respectively, at that date.

Our board of directors granted options to purchase common stock on the above dates, with each option granted on April 27, 2012 or September 11, 2012 having an exercise price of \$50.00 per share and each option granted on September 24, 2013, December 4, 2013 and December 30, 2013, respectively, having an exercise price of \$3.42 per share. In establishing this exercise price, our board of directors considered input from management, including the contemporaneous valuations of our common stock as of January 31, 2012 and August 31, 2013, respectively, as discussed below, as well as objective and subjective factors, including our ongoing operations and market conditions.

In August 2013, based on our review of overall market conditions and the improving market for biopharmaceutical initial public offerings, our board of directors determined that a significant shift was occurring with respect to the valuation we could achieve in an initial public offering and directed us to begin preparation and submission of a confidential draft registration statement for an initial public offering. We selected underwriters and held an organizational meeting in October 2013. We believe these events increased the probability of an early initial public offering scenario and therefore, in connection with the preparation of our financial statements, we re-assessed the fair value of our common stock for financial reporting purposes at interim dates between the contemporaneous valuations where there were stock option grants. For these interim periods, we adjusted the fair value based on market conditions, progress made in our development programs and whether we achieved company milestones. A retrospective valuation was completed as of December 31, 2012.

Common stock valuation

We have historically granted stock options at exercise prices not less than the fair value of our common stock. As there has been no public market for our common stock to date, the estimated fair value of our common stock has been determined by our board of directors. We are a private company with no active public market for our common stock. Therefore, 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 Issued as Compensation* (Practice Aid). We performed these contemporaneous valuations as of January 31, 2012 and August 31,

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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

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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:

- n 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;
- n our results of operations, financial position and the status of research and development efforts;
- n the composition of, and changes to, our management team and board of directors;
- n the lack of liquidity of our common stock as a private company;
- n our stage of development and business strategy and the material risks related to our business and industry;
- n the achievement of enterprise milestones, including entering into collaboration and license agreements;
- n the valuation of publicly traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of peer companies;
- n any external market conditions affecting the life sciences and biotechnology industry sectors;
- n 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;
- n the state of the initial public offering market for similarly situated privately held biotechnology companies; and
- n any recent contemporaneous valuations prepared by our board of directors and management in accordance with methodologies outlined in the Practice Aid.

Common stock valuation methodologies

These contemporaneous and retrospective valuations discussed below were prepared in accordance with the guidelines in the Practice Aid, which prescribes several valuation approaches for setting the value of an enterprise, such as the cost, market and income approaches, and various methodologies for allocating the value of an enterprise to its common stock. We generally used the income and market approaches. When applying the market approach, we used the guideline company and precedent transaction methodologies based on inputs from comparable public companies' equity valuations and comparable acquisition transactions to estimate our enterprise value. In applying the income approach, we applied the discounted cash flow method based on the Company's projections.

Methods used to allocate our enterprise value of classes of securities

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In accordance with the Practice Aid, we considered the various methods for allocating the enterprise value across our classes and series of capital stock to determine the fair value of our common stock at each valuation date. The methods we considered consisted of the following.

Current value method

Under the current value method, once the fair value of the enterprise is established, the value is allocated to the various series of preferred and common stock based on their respective seniority, liquidation preferences or conversion values, whichever is greatest.

Option pricing method

Under the option pricing method, shares are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The values of the preferred and common stock are inferred by analyzing these options.

Probability-weighted expected return method (PWERM)

The PWERM is a scenario-based analysis that estimates the value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us as well as the economic and control rights of each share class.

January 31, 2012 common stock valuation

In the January 31, 2012 contemporaneous valuation, we used the income approach to determine our enterprise value and the option pricing method to allocate the value to the common stock. The option pricing method treats common stock and preferred stock as call options on the enterprise's value, with exercise prices based on the

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liquidation preference of the preferred stock. The common stock has value only if the funds available for distribution to stockholders exceed the value of the liquidation preference at the time of a liquidity event (e.g., merger or sale), assuming the enterprise has funds available to make a liquidation preference meaningful and collectible by the stockholders. The common stock is modeled as a call option that gives its owner the right but not the obligation to buy the underlying enterprise value at a predetermined or exercise price. In the model, the exercise price is based on a comparison with the enterprise value rather than, as in the case of a regular call option, a comparison with a per-share stock price. Thus, common stock is considered to be a call option with a claim on the enterprise at an exercise price equal to the remaining value immediately after the preferred stock is liquidated. Typically option-pricing models such as the Black-Scholes model or a form of a lattice model (e.g., binomial) would be used to price the call option. The option-pricing method considers the various terms of the stockholder agreements upon liquidation of the enterprise, including the level of seniority among the securities, dividend policy, conversion ratios and cash allocations. In addition, the method implicitly considers the effect of the liquidation preference as of the future liquidation date, not as of the valuation date.

In applying the income approach to determine our enterprise value, we utilized the discounted cash flow (DCF) method. The key assumptions utilized in the DCF method were as follows.

- n We prepared a long range projection of our financial results for the years ended December 31, 2012 through 2026.
- n We present valued the projected future cash flows using the weighted average cost of capital (WACC) of 27 percent. The WACC was determined by considering the Capital Asset Pricing Model and the Venture Capital Rate of Return Studies. We utilized the average WACC of the two methodologies.

We allocated the enterprise value determined by the DCF method by utilizing the option pricing method and the key assumptions were as follows.

- n Underlying equity value Determined by the DCF method.
- n Volatility We estimated volatility based on guideline publicly-traded companies with a term consistent with the timeline to the liquidity event.
- n Time to liquidity We estimated a weighted-average time to a sale event of 3.00 years based on the projected time to significant clinical development events for our product candidates.
- n Risk-free interest rate We determined the risk-free interest rate based on the yield of a U.S. Treasury bill with a maturity date closest to the estimated time to a sale event for our stockholders.
- n Discounts for lack of control and marketability The common stock options being granted represent an option to purchase a minority interest in the Company. As our capital structure is comprised of common and preferred stock, we considered the additional rights held by the holders of the preferred stock. The preferred stock possess certain rights not held by the common stockholders. These rights include, but are not limited to, drag-along rights, rights to appoint board members and rights to participate in certain financings. Additionally, as of January 31, 2012, we believed the most likely liquidity event was a trade sale. Because we are a privately-held company, shares of our common stock are highly illiquid and, as such, warrant a discount in value from their estimated marketable price. In assessing the discount, we used legal guidelines from U.S. tax court cases regarding privately-held business valuations, fundamental business factors and empirical studies on the discount for lack of marketability. We corroborated the discount based on the value of a put option compared to the value of common stock using a Black-Scholes option-pricing model. We also considered that our preferred stock has rights that our common stock does not have, including anti-dilution protection, redemption rights, protective provisions in our certificate of incorporation and rights to participate in future rounds of financing. Our preferred stockholders have control and influence over the enterprise, which provides them with the optionality over future liquidity, financing and other decisions that the common stock option holders do not control. As a result of these factors, we applied an aggregate 25 percent discount for lack

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of control and marketability.

The resulting value, which represented the estimated fair value of our common stock as of January 31, 2012, was \$50.00 per share.

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December 31, 2012 retrospective common stock valuation

In the December 31, 2012 retrospective valuation we used the income approach to determine our enterprise value and the option pricing method to allocate the value to the common stock.

In applying the income approach to determine our enterprise value, we utilized the DCF method. The key assumptions utilized in the DCF method were as follows.

- n We prepared a long range projection of our financial results for the years ending December 31, 2013 through 2027.
- n We present valued the projected future cash flows using a WACC of 28 percent. The WACC was determined by using the Capital Asset Pricing Model and the Venture Capital Rate of Return Studies. This increased from the WACC of 27 percent used in the January 31, 2012 valuation to account for the variability in revenue projections.

We allocated the enterprise value determined by the DCF method by utilizing the option pricing method and the key assumptions were as follows.

- n Underlying equity value Determined by the DCF method.
- n Volatility We estimated volatility based on guideline publicly-traded companies with a term consistent with the timeline to the liquidity event.
- n Time to liquidity We estimated a weighted-average time to a sale event of 3.00 years based on the projected time to significant clinical development events for our product candidates.
- n Risk-free interest rate We determined the risk-free interest rate based on the yield of a U.S. Treasury bill with a maturity date closest to the estimated time to a sale event for our stockholders.
- n Discounts for lack of marketability We applied a 25 percent discount for lack of marketability.

The estimated per share fair value of our common stock calculated in our retrospective valuation as of December 31, 2012 of \$15.00 per share decreased from the January 31, 2012 contemporaneous valuation of \$50.00 per share primarily due to the following factors:

- n delay in identifying product candidates; and
- n delay in raising our next round of financing.

August 31, 2013 common stock valuation

The August 31, 2013 contemporaneous valuation was completed after a recapitalization of the Company effected on July 25, 2013. The Series A and Series B preferred stock reverse split ratio was one-for-25 and the common stock reverse split ratio was one-for-250. For the August 31, 2013 valuation, we utilized the hybrid method to value our common stock. Specifically, we used two market approaches, the recent transactions method and guideline initial public offering transactions, and a third scenario, namely sale below the liquidation preference with no value to the common stock, to estimate the value of our equity. In utilizing the recent transactions method, we utilized an option pricing model to estimate

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our equity value, which was consistent with the price paid for the Series C preferred stock acquired by investors on July 30, 2013. In applying the initial public offering scenario, we assumed all of our preferred stock would convert into common stock under the guideline initial public offering transactions method. Under the sale below the liquidation preference scenario, there is no value allocated to the common stock. In each case, we applied probability weightings to the various methodologies based upon our assessment of our prospects of a sale/merger transaction or an initial public offering or the sale below the liquidation preference of our common stock.

For the contemporaneous valuation at August 31, 2013, we used the recent transactions method and the guideline initial public offering method to determine the value of our equity under the sale/merger and initial public offering scenarios. The recent transaction method was used to determine our value under a possible trade sale transaction, and the guideline initial public offering method was used to estimate the equity value under the potential initial public offering scenario. There is no value allocated to the common stock under the sale below liquidation

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preference scenario. The specific facts and circumstances considered by our board of directors in assessing these key valuation assumptions included those noted in the following table.

AUGUST 31, 2013

MAJOR ASSUMPTIONS	INITIAL PUBLIC OFFERING	OPTION PRICING MODEL	SALES BELOW LIQUIDATION PREFERENCE
Probability of scenario	50%	40%	10%
Discount for marketability	10%	10%	N/A
Timeline to liquidity	0.67 years	2.50 years	N/A
Discount rate common stock	30%	N/A	N/A
Estimated per share fair value of common stock before discounts	\$ 5.87	\$ 2.14	\$ 0.00

In applying the market approach to estimate our future enterprise value under the initial public offering exit scenario, as described previously, it was assumed that a liquidity event would occur in 0.67 years. Given our development pipeline and expected clinical trials, as of the valuation date, the selected enterprise value in the initial public offering scenario was based on the pre-money initial public offering market data for transactions between the low and the 25th percentile of the observed range. The selected enterprise value contemplated our stage of development, amount of capital raised, depth of product candidates and number of partnerships and collaborations in comparison to the initial public offering transactions.

In applying the market approach to estimate our aggregate future enterprise value under the option pricing model scenario, as described previously, it was assumed that a liquidity event would occur in 2.50 years. The selected enterprise value utilized in the option pricing model scenario was based on the July 30, 2013 Series C preferred stock financing. In the Series C preferred stock financing, we issued and sold 8,142,891 shares of Series C preferred stock at a purchase price of \$7.00 per share for aggregate proceeds of \$57.0 million. The Series C preferred stock financing was an arm's length transaction with terms, including purchase price, negotiated between us and three investors that, prior to the Series C preferred stock financing, were not related parties and did not hold any shares or other interests in us.

As of June 30, 2013, we had cash and cash equivalents of approximately \$1.8 million, which would have allowed us to continue operations for less than two months. As we were running out of cash and existing investors expressed an unwillingness to invest additional capital, we pursued capital from new investors. In July 2013, we negotiated the Series C preferred stock financing with the three new investors. The terms of the financing required significant dilution to existing investors, management and other existing equity holders, by effecting a one-for-25 reverse split of our Series A and Series B preferred stock and a one-for-250 reverse split of our common stock. We used the back-solve method to determine the value of our common stock as of August 31, 2013, which we considered an appropriate method for such determination as we had completed the recapitalization on July 25, 2013 as a condition to closing of our Series C preferred stock financing.

All of the shares of Series C preferred stock were sold and issued at \$7.00 per share, about half of which were purchased by the new investors and the other half by some of our existing stockholders. We also issued 428,526 shares of Series C preferred stock on the same day in satisfaction of a \$3.0 million bridge loan then outstanding. Holders of Series C preferred stock are entitled to senior rights, preferences and privileges as compared to our common stock, including a dividend preference as, if and when declared by the board of directors, a liquidation preference and a redemption right.

As previously noted, under the sale below liquidation preference scenario there is no value allocated to the common stock.

We applied a discount for lack of marketability of ten percent and ten percent under the initial public offering and option pricing model scenarios, respectively. We assessed the probabilities of each transaction and assigned a 50 percent weighting to the initial public offering scenario, 40 percent to the option pricing model scenario and ten

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percent to the sale below liquidation preference scenario based on our assessment of our development pipeline and market conditions. The resulting value, which represented the estimated fair value of our common stock as of August 31, 2013, was \$3.42 per share.

The estimated per share fair value of our common stock calculated in our valuation as of August 31, 2013 of \$3.42 per share decreased from the December 31, 2012 valuation of \$15.00 per share primarily due to the following factors:

- n the purchase price per share of our Series C preferred stock was \$7.00, a purchase price negotiated on arm's length terms with third parties that were not related parties prior to purchasing shares in the Series C preferred stock financing, and these third parties purchased half of the shares of Series C preferred stock sold by us in the financing;
- n our preferred stock is entitled to certain senior rights, preferences and privileges as compared to our common stock, including a dividend preference as, if and when declared by our board of directors, a liquidation preference and a redemption right;
- n at the time of the Series C preferred stock financing and the August 31, 2013 contemporaneous valuation, the consummation of an initial public offering was a possibility considered by management but it was not considered more likely than continuing to run the business as a private company after the Series C preferred stock financing, and management focused its attention on the use of funds from the Series C preferred stock financing to develop a product candidate to advance out of preclinical development, leaving open the possibility of being acquired by another company or remaining a private company;
- n all of our product candidates are in preclinical development, a stage of development at which it is difficult to obtain substantial private sector equity financing and even more difficult to obtain public financing, in contrast with later stage biopharmaceutical companies, which tend to have a greater number of potential sources of financing; and
- n we were delayed in identifying product candidates, which significantly impacted our ability to demonstrate potential to advance a product candidate out of preclinical development, a key factor in seeking financing from investors in either private or public markets.

Initial public offering price

In consultation with the underwriters for this offering, we determined the price of \$15.00 per share for this offering as set forth on the cover page of this prospectus. In comparison, our estimate of the fair value of our common stock was \$3.42 per share as of August 31, 2013. We note that, as is typical in initial public offerings, the price for this offering was not derived using a formal determination of fair value but was determined by negotiation between us and the underwriters. Among the factors that were considered in setting this price were the following:

- n an analysis of the typical valuation ranges seen in recent initial public offerings for companies in our industry;
- n the general condition of the securities markets and the recent market prices of, and the demand for, publicly traded common stock of generally comparable companies;
- n an assumption that there would be a receptive public trading market for pre-commercial biotechnology companies such as us; and
- n an assumption that there would be sufficient demand for our common stock to support an offering of the size contemplated by this prospectus.

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The price for this offering reflects a significant increase over the estimated valuation as of August 31, 2013 of \$3.42 per share. Investors should be aware of this difference and recognize that the price for this offering is in excess of our prior valuations. Further, investors are cautioned not to place undue reliance on the valuation methodologies discussed above as an indicator of future stock prices. We believe the difference may be due to the following factors.

- n The contemporaneous valuation prepared as of August 31, 2013 contained multiple liquidity scenarios, including an initial public offering with an anticipated completion date of March 2014, to which we

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assigned a probability weighting of 50 percent. However, the consideration of different scenarios accounts for some but not all of the difference between the initial public offering price and the valuation as of August 31, 2013.

- n There have been no negative findings from our research and development programs since August 31, 2013 that would otherwise adversely affect our research and development efforts and reduce the value of our common stock.

- n Improved capital market conditions for companies in our industry, as evidenced by a recent increase in the number of public offerings by such companies and in the initial public offering valuations of such companies compared to the valuations in their most recent pre-initial public offering equity financing.

- n The initial public offering price necessarily assumes that this offering has occurred, a public market for our common stock has been created and that our preferred stock has converted into common stock in connection with this offering. Therefore, the initial public offering price excludes the marketability or illiquidity discounts associated with the timing or likelihood of an initial public offering, the superior rights and preferences of our preferred stock and the alternative scenarios considered in the contemporaneous valuations over the past two years. Our August 31, 2013 valuation included an illiquidity discount of ten percent and ten percent in the initial public offering and option pricing model scenarios, respectively.

- n In the public markets, we believe there are investors who may apply more qualitative and subjective valuation criteria to certain of our technologies and development programs than the valuation methods applied in our valuations, although there can be no assurance that this will in fact be the case. As described above, as a private company, we used a more quantitative methodology to determine the fair value of our common stock and this methodology differs from the methodology used to determine the initial public offering price. The initial public offering price was not derived using a formal determination of fair value, but rather was determined by negotiation between us and the underwriters. In particular, the estimate of fair value of our common stock as of August 31, 2013 was not a factor in setting the initial public offering price.

- n The price that investors are willing to pay in this offering, for which the price is intended to serve as an estimate, may take into account other things that have not been expressly considered in our prior valuations, are not objectively determinable and that valuation models are not able to quantify.

Investors should be cautioned that the initial public offering price set forth on the cover of this prospectus does not necessarily represent the fair value of our common stock but rather reflects the offering price determined in consultation with the underwriters.

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

For the stock options granted on December 4, 2013 and December 30, 2013, our board of directors determined, based on the factors discussed above, 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 this offering, for financial reporting purposes, in early January 2014 we conducted a preliminary 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 this offering of \$11.00 to \$13.00 per share. The preliminary retrospective valuation as of December 31, 2013 indicates that the fair value of our common stock on December 31, 2013 was \$7.42 per share. The 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 the Company has 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 the Company's common stock in the range of \$11.00 to \$13.00 per share in such an initial public offering. We plan to record stock-based compensation charges 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, which will be reflected in our financial statements for the fiscal year ended December 31, 2013.

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There are significant judgments and estimates inherent in the determination of these valuations. These judgments and estimates include assumptions regarding our future performance, including the successful enrollment and completion of our clinical studies as well as the determination of the appropriate valuation methods. If we had made different assumptions, our stock-based compensation expense could have been different. The foregoing valuation methodologies are not the only methodologies available and they will not be used to value our common stock once this offering is complete. We cannot make assurances as to any particular valuation for our common stock. Accordingly, investors are cautioned not to place undue reliance on the foregoing valuation methodologies as an indicator of future stock prices.

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 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.

Results of Operations*Comparison of the nine months ended September 30, 2012 and 2013 (Unaudited)*

The following table summarizes the results of our operations for the nine months ended September 30, 2012 and 2013 (in thousands, except percentages):

	FOR THE NINE MONTHS ENDED SEPTEMBER 30,		INCREASE (DECREASE)	
	2012	2013		
Revenue:				
Option exercise fees and preclinical payments	\$ 346	\$	\$ (346)	(100%)
Mutually agreed upon research	416		(416)	(100%)
Total revenue	762		(762)	(100%)
Expenses:				
Research and development	8,078	7,364	(714)	(9%)
General and administrative	3,631	3,577	(54)	(1%)
Total expenses	11,709	10,941	(768)	(7%)
Loss from operations	(10,947)	(10,941)	6	0%
Other expense	687	858	171	25%
Net loss	\$ (11,634)	\$ (11,799)	\$ (165)	1%

Revenue

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We recognized revenue of \$0.8 million for the nine months ended September 30, 2012 and no revenue for the same period in 2013. The revenue recognized in the first nine months of 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 or had service periods in the first nine months of 2013. We do not expect to generate any product revenue for the foreseeable future.

Research and development expenses

Research and development expenses were \$8.1 million for the nine months ended September 30, 2012 and \$7.4 million for the same period in 2013. The decrease of \$0.7 million, or 9 percent compared to the same period in 2012, was primarily due to a \$0.7 million decrease in employee-related expenses resulting from a realignment and reduction of staff and a \$2.2 million decrease in spending on research and development of DsiRNA molecules and delivery technologies, which were both partially offset by a \$2.2 million increase in DCR-M1711 project-related

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expenses due to a natural shift of resources from our completed EnCore platform towards increased development activities in preparation for a clinical trial for DCR-M1711 that 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 \$3.6 million for the nine months ended September 30, 2012 and \$3.6 million for the same period in 2013. 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 \$0.7 million for the nine months ended September 30, 2012 and \$0.9 million for the same period in 2013. The increase of \$0.2 million, or 29 percent compared to the same period in 2012, was primarily due to the loss on extinguishment in 2013 of \$0.3 million and remeasurement of the warrants exercisable for Series A and Series B preferred stock of \$0.2 million, which were partially offset by a decrease of interest expense by \$0.3 million. The loss on extinguishment relates to the Series C bridge loan that closed in June 2013. The decrease in interest expense was due to a decrease in the Hercules loan balance outstanding at September 30, 2013 as compared to September 30, 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 year ended December 31, 2011 and 2012

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

	FOR THE YEAR ENDED DECEMBER 31,			
	2011	2012	INCREASE (DECREASE)	
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 year ended December 31, 2011 and \$7.0 million for the same period in 2012. Total revenue in both years relates to payments received under 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.

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Research and development expenses

Research and development expenses were \$10.7 million for the year ended December 31, 2011 and \$11.6 million for the same period in 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 year ended December 31, 2011 and \$4.7 million for the same period in 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 year ended December 31, 2011 and \$0.9 million for the same period in 2012. The decrease of \$0.1 million, or 10 percent compared to the same period in 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 September 30, 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 (Series C bridge loan)), \$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 September 30, 2013, our cash and cash equivalents were \$54.7 million and we also had \$0.3 million in restricted cash.

In June 2011, we entered into an amendment to our original loan and security agreement with Hercules Technology II, L.P. (Hercules), pursuant to which we are entitled to borrow a term loan in the principal amount of up to \$12.0 million with a 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 warrant has an exercise price of \$25.00 per share.

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.

In July 2013, we closed on our Series C preferred stock financing and issued 8,142,891 shares of Series C preferred stock for gross proceeds of \$57.0 million and issued 428,526 shares of Series C preferred stock in satisfaction of a \$3.0 million bridge loan financing.

Cash flows

As of September 30, 2013, we had \$54.7 million in cash and cash equivalents and \$0.3 million in restricted cash as well as \$5.9 million in indebtedness. The indebtedness represents the aggregate principal amount under our secured term loan.

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The following table shows a summary of our cash flows for the years ended December 31, 2011 and 2012 and the nine months ended September 30, 2012 and 2013 (in thousands).

	FOR THE YEAR ENDED DECEMBER 31,		FOR THE NINE MONTHS ENDED SEPTEMBER 30,	
	2011	2012	2012	2013
Net cash used in operating activities	\$ (8,866)	\$ (15,737)	\$ (11,567)	\$ (5,315)
Net cash used in investing activities	(501)	(120)	(120)	(192)
Net cash provided by (used in) financing activities	7,255	(2,963)	(1,999)	56,549
Increase (decrease) in cash and cash equivalents	\$ (2,112)	\$ (18,820)	\$ (13,686)	\$ 51,042

Operating activities

Net cash used in operating activities was \$11.6 million and \$5.3 million for the nine months ended September 30, 2012 and 2013. The decrease in cash used in operating activities of \$6.3 million was primarily due to a decrease in our research collaboration and license agreement receivable compared to the first nine months of 2013 related to an option exercise fee and preclinical payments earned in December 2012 but not collected until 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.

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 \$0.2 million for the nine months ended September 30, 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 \$2.0 million for the nine months ended September 30, 2012 relates entirely to repayments on the Hercules loan. Net cash provided by financing activities of \$56.5 million for the nine months ended September 30, 2013 is due to \$60.0 million of proceeds from the issuance of Series C preferred stock (including \$3.0 million of proceeds from our Series C bridge loan and related Series C warrants), which is partially offset by \$3.0 million of repayments on the Hercules loan and \$0.5 million of issuance costs.

Net cash provided by financing activities of \$7.3 million for the year 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 year ended December 31, 2012 relates entirely to repayments on our Hercules loan.

Funding requirements

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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 estimated net proceeds from this offering, together with our existing cash and cash equivalents as of September 30, 2013, but excluding any potential option exercise fees or milestone payments, will be sufficient to meet our anticipated cash requirements through 2015. 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

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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:

- n the receipt of milestone payments under our research collaboration and license agreement with KHK;
- n the terms and timing of any other collaboration, licensing and other arrangements that we may establish;
- n the initiation, progress, timing and completion of preclinical studies and clinical trials for our potential product candidates;
- n the number and characteristics of product candidates that we pursue;
- n the progress, costs and results of our preclinical studies and clinical trials;
- n the outcome, timing and cost of regulatory approvals;
- n delays that may be caused by changing regulatory requirements;
- n the cost and timing of hiring new employees to support our continued growth;
- n the costs involved in filing and prosecuting patent applications and enforcing and defending patent claims;
- n the costs of filing and prosecuting intellectual property rights and enforcing and defending any intellectual property-related claims;
- n the costs and timing of procuring clinical and commercial supplies of our product candidates;
- n the extent to which we acquire or in-license other product candidates and technologies; and
- n the extent to which we acquire or invest in other businesses, product candidates or technologies.

Please see the section titled "Risk Factors" elsewhere in this prospectus 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 public or private equity offerings, debt financings and research collaboration and license agreements. We may be unable to raise capital or enter into such other arrangements when needed or on favorable terms or at all. Our failure to raise capital or enter into such other arrangements 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, 2012 (in thousands).

CONTRACTUAL OBLIGATIONS	TOTAL	PAYMENTS DUE BY PERIOD			
		LESS THAN 1 YEAR	AND LESS THAN 3	MORE THAN 1 YEAR AND LESS THAN 5	MORE THAN 3 YEARS AND MORE THAN 5 YEARS
Short and long-term debt obligations ⁽¹⁾	\$ 9,166	\$ 4,140	\$ 5,026	\$	\$
Interest on short- and long-term debt obligations ⁽²⁾	1,060	751	309		
Operating lease obligations ⁽³⁾	887	887			
Total	\$ 11,113	\$ 5,778	\$ 5,335	\$	\$

⁽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 for accounting purposes.

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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.

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 as of September 30, 2013, we had cash equivalents of \$22.3 million, \$3.2 million and \$54.1 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 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 equivalents. To minimize the risk in the future, we intend to maintain our portfolio of 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.

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.

Table of Contents**BUSINESS****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 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 intend 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 expect to retain substantially all commercial rights in key markets. In oncology and other more prevalent disease areas, we intend to 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.

- n **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. PH1 afflicts an estimated one to three people per million of population and may afflict as many as eight people per million of population and causes severe renal disease and early mortality. 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 intend to begin clinical trials for DCR-PH1 in 2015. We expect to announce initial proof-of-concept clinical data in mid to late 2015.
- n **Other rare inherited diseases involving the liver.** We are investigating a number of other rare diseases involving disease target genes expressed in the liver. These include maple syrup urine disease, familial amyloid polyneuropathy or cardiomyopathy, alpha-1 anti-trypsin hepatocyte inclusions, severe hemophilia A and B and paroxysmal nocturnal hemoglobinuria, among others. In each case, we are seeking to target a clear unmet medical need, a readily-identified patient population, favorable market dynamics, potential orphan drug designation and the possibility to use RNAi-based therapeutics to achieve an optimal combination of high efficacy and low toxicity. Based on the investigation results, we plan to select a specific disease or disorder to further research and develop. We expect to initiate clinical trials in 2015 for any program that we advance into development.
- n **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 and this increased gene expression has been shown to be related to the presence and severity of cancer. 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 and expect to announce initial proof-of-concept clinical data in mid to late 2015. We intend to investigate DCR-M1711 in a variety of tumor types. Our initial focus is on hepatocellular carcinoma (HCC), which we believe represents 85 to 90 percent of primary liver cancer.
- n **Product candidate for KRAS-related cancers in collaboration with KHK.** 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.

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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.

- n **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 increases the efficacy of the RNAi mechanism. This benefit both increases the potency of our DsiRNA molecules relative to other molecules used to induce RNAi and enables many more sequences to be used to generate potent DsiRNAs compared to other RNAi-inducing molecules.
- n **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. Our delivery particles are highly potent, have low toxicity and are amenable to manufacturing in large scale. We have found that, even at doses as low as 13.1µg/kg, we can induce silencing of gene expression at the 50 percent level, which we believe is 100-fold to 1,000-fold 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.
- n **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 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. These agents allow the DsiRNA to be targeted to specific cell types and to enter the cytoplasm of the cell. The targeting agent mediates cell binding and internalization, and the endosomal escape agent mediates 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. RNAi molecules that are not cleaved by Dicer may require the use of cleavable linkers, which are less stable and may be more challenging to

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synthesize into the RNA strands. We have shown 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 will utilize these conjugation points to improve further the delivery of our DsiRNAs. We are currently developing delivery technologies using this approach to deliver directly 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. 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.

Strategy

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

- n **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 will generate human proof-of-concept data. We intend to maximize the likelihood of success in those trials by: (1) using genetic analysis 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 our strong data showing the destruction or knockdown of target mRNA molecules induced by double-stranded RNA molecules at preclinical dose levels will translate into clinical results. We expect to initiate clinical trials for DCR-M1711 in the first half of 2014 and for DCR-PH1 in 2015. We expect to announce initial proof-of-concept clinical data for DCR-M1711 and DCR-PH1 in mid to late 2015.
- n **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, including antithrombin for clotting disorders and AAT for hepatocyte inclusions associated with alpha-1 anti-trypsin deficiency. We are exploring a variety of other rare genetic diseases that we believe offer attractive targets for RNAi therapeutics in the liver. We also continue to explore well known and frequently mutated oncogenes that are critical drivers of cancer formation such as CTNNB1 (also known as β -catenin).
- n **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 key markets. In oncology, we seek to partner our product candidates while retaining meaningful 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.
- n **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 partnerships with pharmaceutical companies across multiple indication areas or in therapeutic areas outside of rare

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diseases and oncology depending on the attractiveness of the opportunities. These partnerships will provide us with validation of our technology platform, funding to advance our proprietary product candidates and access to development, manufacturing and commercial expertise and capabilities.

- n **Continue to invest in our RNAi technology platform.** We will 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, thereby providing 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 inherently more potent than traditional RNAi-inducing molecules. This 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. 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.

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 preferentially to take up the Guide Strand, leading to several advantages for DsiRNAs compared to other RNAi-inducing molecules.

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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 will 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 are less likely to induce an immune system response in humans.

Our optimization process begins with the screening of 300 to 600 DsiRNA sequences predicted to have good activity based on a proprietary DsiRNA prediction algorithm. Through four rounds of optimization and chemical modification, generally taking four to six months, we narrow this group to identify what the results indicate to be the most active molecules while engineering in enhanced stability and engineering out immunostimulatory activity. We routinely achieve high potencies, with IC₅₀ values (the amount of material required to silence a target gene by 50 percent) in the 0.1 to 3.0 picomolar range in *in vitro* studies. Owing to the enzymatic nature of the RNAi pathway, this is 100 to 1,000 times as great as, or greater than, the potency of most traditional small molecule therapeutics.

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 overcome these challenges.

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.

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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 also 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 effective delivery of our DsiRNAs in animal models.

EnCore structure and function

The EnCore lipid nanoparticles are comprised of a Core of lipid and DsiRNA, surrounded by an Envelope of chemically distinct lipids that are designed to interact with the target tissue. The Core allows EnCore to carry a large payload of DsiRNA while simultaneously protecting the DsiRNA from degrading enzymes. The envelope interacts with the target tissue to mediate accumulation, internalization and release into the cytoplasm.

Delivery to the liver and solid tumors with EnCore

By adjusting the lipid components in the EnCore envelope, we have been able to adjust whether EnCore mediates delivery to the liver or to solid tumors in animal models. In each case, the first step of delivery is accumulation in the target tissue. Both liver tissue and tumor tissue have porous vasculature that allows the EnCore lipid nanoparticles to exit the vasculature and accumulate in the target tissue. Our studies to date indicate that other tissues do not accumulate EnCore lipid nanoparticles in significant amounts. EnCore lipid nanoparticles with a low level of polyethylene glycol (PEG) on their surface immediately enter the liver tissue and mediate delivery of DsiRNAs to liver cells. EnCore lipid nanoparticles with a high level of PEG on their surface are blocked from immediate liver uptake, allowing them to continue circulating and to accumulate in tumors. Over time, the PEG is shed from the surface of the EnCore lipid nanoparticles, allowing them to internalize in the tumor cells and mediate delivery of DsiRNAs.

Highly potent delivery of DsiRNA

To demonstrate the efficiency of EnCore in mediating the effective delivery of DsiRNAs, 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 delivered 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 an 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, so the conjugated agents 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 would provide for generalized subcutaneous delivery of DsiRNAs to various cell types throughout the body, as we believe that these molecules should have broad biodistribution, similar to monoclonal antibodies. We expect this system to be ready for formal development and partnering within the next twelve months. We expect that the initial application will be delivery to the liver via conjugation to a GalNAc (n-acetyl galactosamine) targeting agent that provides for highly specific uptake in liver cells that allow for subcutaneous delivery.

The Direct Targeted Delivery system mediates the process of delivery, similar to EnCore, but does so as a single molecular entity instead of a particle. First, the strands of the DsiRNA are conjugated to a targeting agent as well as an agent that allows them to enter the interior of the cell, the cytoplasm, from their delivery vehicle. After delivery to the cell interior, the Dicer enzyme cleaves the molecule just as with an unconjugated DsiRNA.

Our Product Candidates

In choosing clinical programs to pursue using our DsiRNA molecules and drug delivery technologies, we apply the six key criteria listed below.

- n **Strength of therapeutic hypothesis.** Our current product candidate 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. Because our RNAi technology platform allows us to pursue product candidate targets that have historically been difficult to inhibit using conventional approaches, we believe that there are a substantial number of such targets without existing pharmaceuticals on the market or in development.

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- n **Readily-identified patient population.** We seek indications where patients can be readily identified by the presence of characteristic genetic mutations. In the case of genetic diseases, these are heritable genetic traits. In the case of oncology, these are genetic changes that have occurred in tumor cells as part of the tumor-formation process. In both cases, available genetic tests and techniques can identify patients that carry these mutations.

- n **Predictivity of biomarkers for early efficacy assessment.** We seek 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 DsiRNA molecules are likely to have the expected biological and clinical effects in patients.

- n **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.

- n **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. The competitive differentiation has to apply both to therapies based on RNAi as well as to other therapeutic approaches.

- n **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 for use with the potential for rapid development through marketing approval. Specifically, we believe that certain of our product candidates have the potential to obtain Breakthrough Therapy Designation from the U.S. Food and Drug Administration (FDA) as well as accelerated approval.

We believe that our current development programs meet all of these criteria. They reflect a mix of high-value targets and indications that are well suited to our approach.

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

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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. 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 Kuwait, have higher incidences due to founder effects or consanguinity. We believe approximately 400 patients are currently in 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 high oxalate levels 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. These studies demonstrate that genetic deletion of the enzyme prior to AGT1 in the pathway prevents the formation of the oxalate precursor and the buildup of oxalate. 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.

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. We then intend 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 the animal model of PH1.

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Additional liver targets and programs under investigation

We are investigating a number of other rare diseases involving disease target genes expressed in the liver. These include maple syrup urine disease (target: BCKDK (3-methyl-2-oxobutanoate dehydrogenase lipoamide kinase)), familial amyloid polyneuropathy/cardiomyopathy (target: transthyretin), alpha-1 anti-trypsin hepatocyte inclusions (target: alpha-1 anti-trypsin), severe hemophilia A and B (target: antithrombin III) and paroxysmal nocturnal hemoglobinuria (target: complement C5), among others. In each case, we are seeking to target a clear unmet medical need, a readily-identified patient population, favorable market dynamics, potential orphan drug designation and the possibility to use RNAi-based therapeutics to achieve an optimal combination of high efficacy and low toxicity. Based on the investigation results, we plan to select a specific disease or disorder to further research and develop. We expect to initiate clinical trials in 2015 for any program that we advance into development.

DCR-M1711 in hepatocellular carcinoma (HCC)

We believe that our liver cancer product DCR-M1711 has the potential to be used broadly in solid tumors from many tissues of origin, based on observed patterns of MYC amplification. This suggests a large potential market for DCR-M1711. 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

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estimates that more than 414,000 HCC patients will be 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 believe that HCC presents an excellent starting point for clinical development of an MYC-related therapeutic. First, HCC patients frequently show amplifications of the MYC oncogene, suggesting an 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 there is no FDA approved chemotherapeutic regime. Nexavar (marketed by Amgen Inc. and Bayer AG) is the only effective drug for the treatment of advanced or 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.

Since its approval in 2007, Nexavar has substantially increased sales in the HCC market. According to BioMedTracker, annual Nexavar sales exceeded \$1.0 billion in 2012. These sales are largely attributable to the HCC segment, which accounted for approximately \$780.0 million of 2012 sales. Given the high unmet medical need and the relative scarcity of effective HCC therapeutics, we believe that new therapeutic approaches approved for HCC have the opportunity to achieve rapid market adoption.

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.

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, resulting 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.

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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 which 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 this animal model data is supportive of 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, MYC has not been successfully approached by conventional small molecule drugs and is not amenable to antibody therapeutics. Others have attempted to develop small molecules that inhibit MYC but to date these have not been sufficiently potent and specific to be viable product candidates. We believe that the reason for this is likely due to the absence of a good binding pocket on the MYC protein. MYC's role is as a transcription factor and such molecules generally lack binding pockets. Antibodies are not a good option against MYC since they cannot enter the cell at all, and MYC is only found inside the cell.

Over thirty years after the discovery of MYC and numerous attempts to inhibit MYC function with small molecules, oncologists and patients are still in need of a therapeutic agent that can reduce MYC expression. We believe that our platform has this potential capability.

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

We have conducted extensive preclinical studies that have demonstrated that DCR-M1711 shows efficacy in tumor-bearing animals, while demonstrating good tolerability in multiple animal species, including non-human primates. We have directly observed up to 70 percent reductions in the presence of the MYC oncogene transcript in xenograft-bearing animal 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.

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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 shows strong efficacy after DCR-M1711 treatment. 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. The second part will consist of an expansion cohort treated at the maximum tolerated dose.

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. Secondary objectives of the trial are planned to include: (1) observing a direct impact of DCR-M1711 on the MYC mRNA transcript by observing the cleavage products that result from DCR-M1711-guided cleavage of the MYC message by cellular RNAi machinery; (2) observing decreases in the level of MYC transcript when comparing pre- and post-treatment biopsies of tumor tissues; (3) observing a decrease in tumor metabolic activity by imaging techniques, as would be expected from inhibition of MYC function in tumors; and (4) evaluating any evidence of anti-tumor activity in patients treated with DCR-M1711. 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 will be added to the study during the dose escalation or expansion portions of the trial if needed to meet enrollment goals.

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 a maximum tolerated dose when administered in a cycle of three weekly infusions followed by one week without an infusion. Secondary objectives of the trial include: (1) observing a direct impact of DCR-M1711 on the MYC mRNA transcript by observing the cleavage products that result from DCR-M1711-guided cleavage of the MYC message by the cellular RNAi machinery; (2) observing decreases in the level of MYC transcript when comparing pre- and post-treatment

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biopsies of tumor tissues; (3) observing decreases in tumor metabolic activity by imaging techniques, as would be expected from inhibition of MYC function in tumors; and (4) evaluating any evidence of anti-tumor activity in patients treated with DCR-M1711. We are evaluating where to begin enrolling patients in this trial and are likely to conduct this trial in one or more East Asian countries, such as South Korea and Taiwan. 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.

As with most Phase 1 trials, ours will not be designed to yield statistically significant efficacy or molecular marker results. Accordingly, any observed results may be due to chance and not efficacy of DCR-M1711. The principal purpose of our Phase 1 trials will be to provide the basis for design of larger, definitive 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 selection of 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 is highly 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.

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 will 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

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Like MYC, KRAS has historically 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 meaningful results. 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.

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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.

Studies have shown that disruptions to the Ras-MAP Kinase pathway, either by mutations in KRAS or other components of the pathway, are frequent contributors to the development of cancer in humans. Certain mutations in KRAS promote cancer by putting the KRAS protein into a constitutively active state, which promotes the uncontrolled cell growth and division that is the hallmark of cancer. We believe that a therapeutic that can silence the mutant, activated KRAS oncogene should reduce or prevent cancer growth and may have a beneficial effect for patients. Therapeutics have been successfully developed against other components of the Ras-MAP Kinase pathway. For example, receptor tyrosine kinases proteins, which are upstream of KRAS in the Ras-MAP Kinase pathway, are the target of numerous small molecule and antibody drugs currently used to treat certain cancers. In certain cases, it is known that drugs targeting receptor tyrosine kinases are ineffective against tumors which bear an activating mutation in KRAS. For this reason, we believe that our KRAS-targeted DsiRNA molecule can be an effective therapeutic.

Despite its obvious attractiveness as a therapeutic target, KRAS has not been successfully approached by any conventional small molecule and is not amenable to an antibody therapeutic. Others have attempted to generate small molecules that inhibit KRAS but these have not been either sufficiently potent and/or sufficiently specific to be developed as pharmaceuticals, although these efforts continue. The reason for this is likely due to the absence of a good binding pocket on the KRAS protein. Antibodies are not a good option against KRAS since they cannot enter the cell at all, and KRAS is only found inside the cell.

Since the discovery of KRAS thirty years ago and after many attempts to develop drugs targeting KRAS function, oncologists and patients are still in need of a therapeutic agent that can reduce KRAS expression. We believe that our platform has this capability.

Preclinical data for product candidate for KRAS-related solid tumors

KRAS was the first target program initiated at Dicerna. It 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

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.

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The KRAS DsiRNAs and formulations have shown good 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 rule out the activity of any residual immunologic activity in the mice. Taken together, this data set demonstrates with a high degree of certainty that this 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 observed 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.

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.

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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 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.

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Intellectual Property

We invest significant amounts in research and development. Our research and development expenses were approximately \$8.0 million, \$10.7 million and \$11.6 million in 2010, 2011 and 2012, 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 (β -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 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

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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.

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.

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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.

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. Alnylam Pharmaceuticals, Inc. 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 therapies for other indications, including hemophilia, porphyria, hypercholesterolemia, hemoglobinopathies, and alpha-1-antitrypsin (AAT) deficiency hepatocyte inclusions, among others. 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 diseases of the liver and is in Phase 1 studies for HBV. 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 mRNAs copied from them. Companies such as miRagen Therapeutics, Inc., Mirna Therapeutics, Inc., Regulus Therapeutics Inc. and Santaris Pharma A/S utilize microRNAs, which are 15 to 22 nucleotide, short, non-coding RNAs, to interact with mRNAs and inactivate gene expression. The product candidates being developed by these companies are currently in preclinical 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. Tekmira has announced that it expects to initiate a multi-center, single arm, open label dose escalation Phase 1/2 study for TKM-PLK1 in HCC in the first half of 2014.

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 vitamin B6 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 overexpressed.

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 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.

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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:

- n refusal to approve pending applications;
- n withdrawal of an approval;
- n imposition of a clinical hold;
- n warning letters;
- n product seizures;
- n total or partial suspension of production or distribution; or
- n 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:

- n completion of nonclinical laboratory tests, animal studies and formulation studies conducted according to Good Laboratory Practices (GLPs) or other applicable regulations;
- n submission to the FDA of an Investigational New Drug (IND) application, which must become effective before human clinical trials may begin;
- n 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;
- n submission to the FDA of an NDA;
- n 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

ⁿ 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.

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.

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

- n 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.

- n 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.

- n 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.

According to published guidance on the SPA process, a sponsor which meets the prerequisites may make a specific request for a SPA and provide information regarding the design and size of the proposed clinical trial. The FDA is supposed to evaluate the protocol within 45 days of the request to assess whether the proposed trial is adequate, which evaluation may result in discussions and a request for additional information. A SPA request must be made before the proposed trial begins, and all open issues must be resolved before the trial begins. If a written agreement is reached, it will be documented and made part of the record. The agreement will be binding on the FDA and may not be changed by the sponsor or the FDA after the trial begins except with the written agreement of the sponsor and the FDA or if the FDA determines that a substantial scientific issue essential to determining the safety or efficacy of the product candidate was identified after the testing began.

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 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

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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 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

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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 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.

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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 September 30, 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 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:

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

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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.

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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.

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

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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 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:

- n our research and development programs;

- n the design and implementation of our clinical programs;

- n our patent and publication strategies;

- n new technologies relevant to our research and development programs; and

- n 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
Carlo Croce, M.D.	Professor and Chair, Institute of Genetics at Ohio State University
James C. Jenson, Ph.D.	Co-Founder of Dicerna
C. Ronald Kahn, M.D.	Mary K. Iacocca, Professor at Harvard Medical School and Vice Chair, Joslin Diabetes Center
Frank McCormick, Ph.D., F.R.S., D.Sc. (Hon)	Director, University of California, San Francisco Helen Diller Family Comprehensive Cancer Center
Thomas M. Roberts, Ph.D.	Department Co-Chair, Dana-Farber Cancer Institute and Professor at 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 September 30, 2013, we had 24 full-time employees, of whom 18 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.

Facilities

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 our existing facilities are adequate for our current needs and have sufficient laboratory space to house additional scientists as we grow. When our lease expires, we may exercise our renewal options or look for additional or alternate space for our operations. We believe that suitable additional or alternative space will be available in the future on commercially reasonable terms.

Legal Proceedings

We are not currently a party to any material legal proceedings.

Table of Contents**MANAGEMENT****Executive Officers and Directors**

The following sets forth information about our executive officers and directors as of December 31, 2013.

NAME	POSITION	AGE
Douglas M. Fambrough, III, Ph.D.	Chief Executive Officer, Director	45
Brian K. Halak, Ph.D. ⁽²⁾	Director	42
Stephen J. Hoffman, M.D., Ph.D. ⁽¹⁾⁽²⁾	Director	59
Peter Kolchinsky, Ph.D. ⁽³⁾	Director	37
Dennis H. Langer, M.D., J.D. ⁽²⁾	Director	62
David M. Madden ⁽¹⁾⁽³⁾	Chairman	51
Vincent J. Miles, Ph.D. ⁽¹⁾⁽³⁾	Director	63
Bob D. Brown, Ph.D.	Chief Scientific Officer, Senior Vice President	49
James E. Dentzer	Chief Financial Officer	47
James B. Weissman	Chief Business Officer	51

⁽¹⁾ Member of the audit committee, upon completion of this offering.

⁽²⁾ Member of the compensation committee, upon completion of this offering.

⁽³⁾ Member of the nominating and corporate governance committee, upon completion of this offering.

The following is information about the experience and attributes of the members of our board of directors and executive officers as of the date of this prospectus. Together, the experience and attributes discussed below provide the reasons that these individuals were selected for board membership, as well as why they continue to serve in such positions.

Douglas M. Fambrough, III, Ph.D., chief executive officer and director

Dr. Fambrough has served as a member of our board of directors since April 2007 and as our chief executive officer since May 2010. From 2000 to May 2010, Dr. Fambrough held various positions at Oxford Bioscience Partners, a life science venture capital firm, most recently as a general partner. During his years at Oxford Bioscience Partners, he specialized in financing innovative life science technology companies, including Sirna Therapeutics, Inc. (acquired by Merck & Co., Inc.), Solexa, Inc. (acquired by Illumina, Inc.), and Cambrios Technologies Corp. Before joining Oxford Bioscience Partners, he was a genomic scientist at the Whitehead/MIT Center for Genome Research (now known as the Broad Institute). Dr. Fambrough graduated from Cornell University and obtained his Ph.D. in genetics at the University of California, Berkeley. We believe that Dr. Fambrough's experience serving as our chief executive officer and a member of our board of directors, combined with his experience in the venture capital industry and biotechnology research and development, provide him with the qualifications and skills to serve as a member of our board of directors.

Brian K. Halak, Ph.D., director

Dr. Halak has served as a member of our board of directors since August 2010. Dr. Halak is currently a partner of Domain Associates, LLC, which he joined in 2001. Prior to joining Domain Associates, LLC, Dr. Halak was an associate with Advanced Technology Ventures. Prior to

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that, Dr. Halak was a consultant at the Wilkerson Group. Dr. Halak currently serves as a member of the boards of directors of Alimera Sciences, Inc. (NASDAQ: ALIM), BioNano Genomics, Inc., Carticcept Medical, Inc., Corridor Pharmaceuticals, Inc., Domain Elite, Kona Medical, Inc. and Oraya Therapeutics Inc. He previously served on the boards of directors of Eddingpharm, Esprit Pharma, Inc. (acquired by Allergan, Inc.), GI Dynamics, Inc. (ASX: GID) and Vanda Pharmaceuticals, Inc. (NASDAQ: VNDA). Dr. Halak received his BSE in bioengineering from the University of Pennsylvania and his Ph.D. in immunology from the Thomas Jefferson University. We believe that Dr. Halak's experience in the venture capital industry, particularly with biopharmaceutical companies, and his experience serving on the boards of directors of a number of biopharmaceutical companies provide him with the qualifications and skills to serve as a member of our board of directors.

Table of Contents***Stephen J. Hoffman, M.D., Ph.D., director***

Dr. Hoffman has served as a member of our board of directors since November 2007. Dr. Hoffman is currently a managing director at Skyline Ventures, a venture capital firm, which he joined in April 2007. From January 2003 to March 2007, Dr. Hoffman was a general partner at TVM Capital, a venture capital firm. From 1994 to 2002, he served as president and chief executive officer and as a member of the board of directors of Allos Therapeutics, Inc. (acquired by Spectrum Pharmaceuticals, Inc.). From 1990 to 1994, Dr. Hoffman completed a fellowship in clinical oncology and a residency/fellowship in dermatology, both at the University of Colorado. Dr. Hoffman was the scientific founder of Somatogen Inc. (acquired by Baxter International Inc.), where he held the position of vice president of science and technology from 1987 until 1990. Dr. Hoffman currently serves on the boards of directors of several biopharmaceutical companies, including AcelRX Pharmaceuticals, Inc. (NASDAQ: ACRX), Collegium Pharmaceuticals, Inc., Concert Pharmaceuticals, Inc., Genocera Biosciences, Inc. and Proteon Therapeutics, Inc. Previously, Dr. Hoffman served on the boards of directors of Allos Therapeutics, Inc. (acquired by Spectrum Pharmaceuticals, Inc.) and Sirtris Pharmaceuticals, Inc. (acquired by GlaxoSmithKline plc (NYSE: GSK)). Dr. Hoffman holds a Ph.D. in bio-organic chemistry from Northwestern University and an M.D. from the University of Colorado School of Medicine. We believe that Dr. Hoffman's scientific and business experience, including his diversified background as an executive officer, director and venture capital investor in biopharmaceutical companies, provide him with the qualifications and skills to serve as a member of our board of directors.

Peter Kolchinsky, Ph.D., director

Dr. Kolchinsky has served as a member of our board of directors since July 2013. Dr. Kolchinsky is a founding partner and portfolio manager at RA Capital, where he has been since September 2004. He is active in both public and private investments across the pharmaceutical, medical devices, diagnostics and life-science tools industries. Dr. Kolchinsky authored the e-book *The Entrepreneur's Guide to a Biotech Startup*, serves on the board of directors of the American Fertility Association and is a member of the board of directors of several private healthcare companies, including CellScape Corporation, Calimmune, Inc. and PiloFocus Inc. In the past, Dr. Kolchinsky served on the Board of Global Science and Technology for the National Academies of Sciences. He received a Ph.D. in virology from Harvard University and a bachelor's degree from Cornell University. We believe that Dr. Kolchinsky's experience as a venture capital investor in and director of a number of healthcare and life sciences companies provides him with the qualifications and skills to serve as a member of our board of directors.

Dennis H. Langer, M.D., J.D., director

Dr. Langer has served as a member of our board of directors since November 2007. Since January 2013, Dr. Langer has served as the chairman of the board of directors and chief executive officer of AdvanDx, Inc. Dr. Langer has been a clinical professor in the department of psychiatry at Georgetown University School of Medicine since September 2003. From August 2005 to May 2010, Dr. Langer served as managing partner of Phoenix IP Ventures, LLC. From January 2004 to July 2005, he served as president, North America of Dr. Reddy's Laboratories, Inc. (NYSE: RDY). From September 1994 until January 2004, Dr. Langer held several positions at GlaxoSmithKline plc (NYSE: GSK) and its predecessor, SmithKline Beecham, culminating with senior vice president of research and development. Dr. Langer currently serves on the board of directors of Myriad Genetics, Inc. (NASDAQ: MYGN). Dr. Langer previously served on the boards of directors of Auxilium Pharmaceuticals, Inc., Cytogen Corporation (acquired by EUSA Pharma, Inc.), Myrexix, Inc., Pharmacopeia, Inc. (acquired by Ligand Pharmaceuticals Incorporated) and Sirna Therapeutics, Inc. (acquired by Merck & Co., Inc.). Dr. Langer received a J.D. (cum laude) from Harvard Law School, an M.D. from Georgetown University School of Medicine and a B.A. in biology from Columbia University. We believe that Dr. Langer's business and management experience, including senior positions at global pharmaceutical companies and innovative research and development experience at companies such as Eli Lilly & Co. (NYSE: LLY), Abbott Laboratories (NYSE: ABT) and G.D. Searle & Company, as well as his diversified background serving as a director of several pharmaceutical companies provide him with the qualifications and skills to serve as a member of our board of directors.

David M. Madden, chairman

Mr. Madden has served as a member and the chairman of our board of directors since June 2009. Mr. Madden is a founder and principal of Narrow River Management, LP, an investment management company with a focus on equity investments in the emerging pharmaceutical industry, where he has been since 2004. Mr. Madden has served as chief executive officer and a member of the board of directors of River Vision Development Corporation since 2011. Mr. Madden also serves as a member of the board of directors of the Hospital for Special Surgery. Mr. Madden

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previously served as interim president and chief executive officer of Adolor Corporation (NASDAQ: ADLR) from August 2005 to December 2006 and the chairman of its board of directors until it was acquired by Cubist Pharmaceuticals, Inc. (NASDAQ: CBST) in December 2011. Mr. Madden was co-chief executive officer of Royalty Pharma AG, a private investment management firm specializing in the acquisition of royalty interests in pharmaceutical products, from October 2000 to 2003, and a member of its board of directors until March 2004. From 1997 to October 2000, he served as a managing member of Pharmaceutical Partners, LLC. From 1992 to 1995, Mr. Madden was president and chief executive officer and a member of the board of directors of Selectide Corporation. Mr. Madden has a B.S. in Electrical Engineering from Union College and an M.B.A. from Columbia University. We believe that Mr. Madden's diversified experience in the pharmaceutical, healthcare and financial services industries, particularly his experience of serving as an executive officer and director of several pharmaceutical companies, provide him with the qualifications and skills to serve as a member of our board of directors.

Vincent J. Miles, Ph.D., director

Dr. Miles has served as a member of our board of directors since November 2013. Dr. Miles is an executive partner of Abingworth, a venture capital firm in the life sciences and healthcare sectors. Before joining Abingworth, Dr. Miles was senior vice president, business development, of Alnylam Pharmaceuticals, Inc. (NASDAQ: ALNY) from 2003 to 2007. From 1997 to 2003, Dr. Miles held various positions at Millennium Pharmaceuticals, Inc., including vice president positions in business development, strategic planning and scientific affairs. Prior to that, Dr. Miles served as the director of the Office of Technology Transfer, Dana Farber Cancer Institute from 1996 to 1997, and vice president of various research and development and business functions at RiboGene, Inc. (a predecessor of Questcor Pharmaceuticals (NASDAQ: QCOR)) from 1992 to 1996 and at Pharmacia P-L Biotech Inc. from 1986 to 1992. Dr. Miles currently serves on the boards of directors of PrimeraDx, Inc., Hydra Biosciences, Inc. and Chiasma, Inc. Dr. Miles holds a B.Sc. in biochemistry and Ph.D. in biochemical embryology from University College London. We believe that Dr. Miles' scientific and business experience serving as an executive officer, director and venture capital investor in biopharmaceutical companies provides him with the qualifications and skills to serve as a member of our board of directors.

Bob D. Brown, Ph.D., chief scientific officer, senior vice president

Dr. Brown initially served as our senior vice president of research beginning in May 2008 and has served as our chief scientific officer since January 2012. From March 2003 to March 2008, Dr. Brown held various positions at Genta Incorporated, most recently as its vice president of research and technology. Previously, he was a co-founder and vice president of research and development of Oasis Biosciences Inc., which was acquired by Gen-Probe Incorporated. Dr. Brown is an inventor or co-inventor on 16 issued patents and dozens of patent applications covering oligonucleotide and conventional small molecule therapeutic agents, diagnostic tool and oligonucleotide and small molecule drug delivery technologies. Dr. Brown holds a Ph.D. in molecular biology from the University of California, Berkeley, and a B.S. in chemistry and biology from the University of Washington, Seattle.

James E. Dentzer, chief financial officer

James E. Dentzer joined us as chief financial officer in December 2013. Prior to that, he was the chief financial officer of Valeritas, Inc. from March 2010 to December 2013, where he led the finance team in raising a \$150 million Series C equity round and a \$100 million debt financing and helped guide the company through approval by the U.S. Food and Drug Administration, manufacturing scale-up and commercial launch of the V-Go insulin delivery device. Prior to joining Valeritas, Inc., he was the chief financial officer of Amicus Therapeutics, Inc. (NASDAQ: FOLD) from October 2006 to October 2009, where he led the company through a Series D preferred stock financing and subsequent initial public share offering. In prior positions, he spent six years as corporate controller of Biogen Idec and six years in various senior financial roles at E.I. du Pont de Nemours and Company in the U.S. and Asia. Mr. Dentzer holds a B.A. in philosophy from Boston College and an M.B.A. from the University of Chicago.

James B. Weissman, chief business officer

Mr. Weissman has served as our chief business officer since January 2012. From January 2006 to January 2012, Mr. Weissman was senior director and then vice president, business development of MannKind Corporation (NASDAQ: MNKD), where he was responsible for leading the company's activities related to licensing, new products and strategic planning. Prior to MannKind, Mr. Weissman held leadership positions in both business development and marketing at Pfizer Pharmaceuticals, Inc. in Tokyo, most recently as senior director of marketing, responsible for the sales, profit and strategic targets for the company's specialty products, in a variety of therapeutic areas. Mr. Weissman holds a B.S. from Bates College in Maine.

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Board Composition

Upon completion of this offering, our board of directors will consist of seven members. Our amended and restated certificate of incorporation will provide that the number of directors may be changed only by resolution of the board of directors. Our board of directors has determined that all of the members of our board of directors, except our chief executive officer, Dr. Fambrough, are independent directors as defined in applicable rules of the Securities and Exchange Commission and The NASDAQ Global Select Market. All directors will hold office until their successors have been elected and qualified or appointed or the earlier of their death, resignation or removal. Executive officers are appointed and serve at the discretion of the board of directors. There are no family relationships among any of our directors or executive officers.

Voting Arrangements

Pursuant to an amended and restated stockholders agreement that we entered into with certain holders of our common stock and certain holders of our preferred stock:

- n Skyline Venture Partners V, L.P. has the right to designate a director for election to our board of directors and has designated Dr. Hoffman as such director;
- n Abingworth Bioventures V, L.P. has the right to designate a director for election to our board of directors and has designated Dr. Miles as such director;
- n Domain Partners VIII, L.P. has the right to designate a director for election to our board of directors and has designated Dr. Halak as such director;
- n RA Capital Healthcare Fund, LP and its affiliates has the right to designate a director for election to our board of directors and has designated Dr. Kolchinsky as such director;
- n our current chief executive officer has the right to be nominated to serve on our board of directors; and
- n a majority of the holders of our common stock and preferred stock have the right to designate two persons for election to our board of directors and have designated Dr. Langer and Mr. Madden.

The holders of our common stock and preferred stock that are parties to the amended and restated stockholders agreement are obligated to vote for such designees. The provisions of the stockholders agreement will terminate upon the consummation of this offering and there will be no further contractual obligations regarding the election of our directors.

Director Independence

Upon the consummation of this offering, our common stock will be listed on The NASDAQ Global Select Market. Under the rules of The NASDAQ Stock Market LLC (NASDAQ), independent directors must comprise a majority of a listed company's board of directors within twelve months from the date of listing. In addition, NASDAQ rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent. Audit committee members must also satisfy additional independence criteria set forth in Rule 10A-3 under the Securities Exchange Act of 1934, as amended (Exchange Act), and in NASDAQ rule 5605(c)(2)(A). Under NASDAQ rules, a director will only qualify as an independent director if, in the opinion of that company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

To be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors or any other board committee, accept, directly or indirectly, any consulting,

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advisory or other compensatory fee from the listed company or any of its subsidiaries or be an affiliated person of the listed company or any of its subsidiaries.

Prior to the completion of this offering, our board of directors undertook a review of its composition, the composition of its committees and the independence of each director. Based upon information requested from and provided by each director concerning his background, employment and affiliations, including family relationships, our board of directors has determined that none of Dr. Halak, Dr. Hoffman, Dr. Kolchinsky, Dr. Langer, Mr. Madden or Dr. Miles, representing six of our seven directors, has a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is independent as that term is defined under NASDAQ rules. Our board of directors has also determined that Dr. Hoffman, Dr. Miles and

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Mr. Madden, who will be members of our audit committee upon completion of this offering, Dr. Halak, Dr. Hoffman and Dr. Langer, who will be members of our compensation committee upon completion of this offering, and Dr. Kolchinsky, Mr. Madden and Dr. Miles, who will be members of our nominating and corporate governance committee upon completion of this offering, satisfy the independence standards for those committees established by applicable Securities and Exchange Commission and NASDAQ rules. Dr. Hoffman and Dr. Miles, each of whom will serve as a member of our audit committee upon completion of this offering, may not qualify as independent under the audit committee independence standards established by the Securities and Exchange Commission and NASDAQ rules if Skyline Venture Partners, in the case of Dr. Hoffman, or Abingworth, in the case of Dr. Miles, continues to own more than ten percent of our capital stock after this offering. In such event, under applicable exemptions in NASDAQ rules, Dr. Hoffman or Dr. Miles, as applicable, would be permitted to continue to serve on the audit committee for up to one year following the consummation of this offering. (For more information, see the section titled "Principal Stockholders" elsewhere in this prospectus.) In making these determinations, our board of directors considered the relationships that each non-employee director has with us and all other facts and circumstances our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director.

Board Diversity

Upon completion of our initial public offering, our nominating and corporate governance committee will be responsible for reviewing with the board of directors, on an annual basis, the appropriate characteristics, skills and experience required for the board of directors as a whole and its individual members. In evaluating the suitability of individual candidates (both new candidates and current members), the nominating and corporate governance committee, in recommending candidates for election, and the board of directors, in approving (and, in the case of vacancies, appointing) such candidates, will take into account many factors, including the following:

- n diversity of personal and professional background, perspective and experience;
- n personal and professional integrity, ethics and values;
- n experience in corporate management, operations or finance, such as serving as an officer or former officer of a publicly held company, and a general understanding of marketing, finance and other elements relevant to the success of a publicly-traded company in today's business environment;
- n experience relevant to our industry and with relevant social policy concerns;
- n experience as a board member or executive officer of another publicly held company;
- n relevant academic expertise or other proficiency in an area of our operations;
- n practical and mature business judgment, including ability to make independent analytical inquiries;
- n promotion of a diversity of business or career experience relevant to our success; and
- n any other relevant qualifications, attributes or skills.

Currently, our board of directors evaluates, and following the completion of our initial public offering will evaluate, each individual in the context of the board of directors as a whole, with the objective of assembling a group that can best maximize the success of the business and represent stockholder interests through the exercise of sound judgment using its diversity of experience in these various areas.

Board Committees

Our board of directors has established the committees described below and may establish others from time to time. The charters for each of our committees will be available on our website once our company is public.

Audit committee

Upon completion of this offering, our audit committee will be comprised of Dr. Hoffman, Mr. Madden and Dr. Miles. Dr. Hoffman will serve as the chairperson of the committee. Our board of directors has determined that each member of the audit committee is independent for audit committee purposes as that term is defined in the applicable rules of the Securities and Exchange Commission and The NASDAQ Global Select Market. Our board of directors has designated Dr. Hoffman as an audit committee financial expert, as defined under the applicable rules of the Securities and Exchange Commission. The audit committee's responsibilities will include:

- n appointing, approving the compensation of and assessing the independence of our independent registered public accounting firm;

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- n pre-approving auditing and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- n reviewing annually a report by the independent registered public accounting firm regarding the independent registered public accounting firm's internal quality control procedures and various issues relating thereto;
- n reviewing and discussing with management and the independent registered public accounting firm our annual and quarterly financial statements and related disclosures;
- n coordinating the oversight and reviewing the adequacy of our internal control over financial reporting with both management and the independent registered public accounting firm;
- n establishing policies and procedures for the receipt and retention of accounting related complaints and concerns, including a confidential, anonymous mechanism for the submission of concerns by employees;
- n periodically reviewing legal compliance matters, including any securities trading policies, periodically reviewing significant accounting and other financial risks or exposures to our company and reviewing and, if appropriate, approving all transactions between our company and any related party (as described in Item 404 of Regulation S-K promulgated under the Exchange Act);
- n establishing policies for the hiring of employees and former employees of the independent registered public accounting firm; and
- n preparing the audit committee report required by Securities and Exchange Commission rules to be included in our annual proxy statement.

The audit committee will have the power to investigate any matter brought to its attention within the scope of its duties and will have the authority to retain counsel and advisors to fulfill its responsibilities and duties.

Compensation committee

Upon completion of this offering, our compensation committee will be comprised of Dr. Halak, Dr. Hoffman and Dr. Langer. Dr. Halak will serve as the chairperson of the committee. Our board of directors has determined that each member of the compensation committee is an independent director for compensation committee purposes as that term is defined in the applicable rules of The NASDAQ Global Select Market, is a non-employee director within the meaning of Rule 16b-3(d)(3) promulgated under the Exchange Act and is an outside director within the meaning of Section 162(m) of the Internal Revenue Code, as amended. The compensation committee's responsibilities will include, among other things:

- n reviewing and approving corporate goals and objectives relevant to the compensation of our chief executive officer;
- n evaluating the performance of our chief executive officer in light of such corporate goals and objectives and approving the compensation of our chief executive officer;
- n reviewing and approving the compensation of our other executive officers;

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- n reviewing our compensation, welfare, benefit and pension plans and similar plans;

- n reviewing and making recommendations to the board of directors with respect to director compensation; and

- n preparing for inclusion in our proxy statement the report, if any, of the compensation committee required by the Securities and Exchange Commission.

The compensation committee will have the power to investigate any matter brought to its attention within the scope of its duties and will have the authority to retain counsel and advisors to fulfill its responsibilities and duties.

Nominating and corporate governance committee

Upon completion of this offering, we will have a nominating and corporate governance committee comprised of Dr. Kolchinsky, Mr. Madden and Dr. Miles. Dr. Kolchinsky will serve as the chairperson of the committee. Our board of directors has determined that each of the committee members is an independent director for nominating and corporate governance committee purposes as that term is defined in the applicable rules of The NASDAQ Global Select Market. The nominating and corporate governance committee's responsibilities will include, among other things:

- n developing and recommending to the board of directors criteria for membership on the board of directors and committees;

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- n identifying individuals qualified to become members of the board of directors;
- n recommending to the board of directors the persons to be nominated for election as directors and to each committee of the board of directors;
- n annually reviewing our corporate governance guidelines; and
- n monitoring and evaluating the performance of the board of directors and leading the board in an annual self-assessment of its practices and effectiveness.

The nominating and corporate governance committee will have the power to investigate any matter brought to its attention within the scope of its duties and will have the authority to retain counsel and advisors to fulfill its responsibilities and duties.

Risk Assessment and Compensation Practices

Our management assessed and discussed with our compensation committee our compensation policies and practices for our employees as they relate to our risk management and, based upon this assessment, we believe that any risks arising from such policies and practices are not reasonably likely to have a material adverse effect on us in the future.

Our employees' base salaries are fixed in amount and thus we do not believe that they encourage excessive risk taking. While performance-based cash bonuses focus on achievement of short-term or annual goals, which may encourage the taking of short-term or annual risks at the expense of long-term results, we believe that our compensation policies help mitigate this risk and our performance-based cash bonuses are limited, representing a small portion of the total compensation opportunities available to most employees. We also believe that our performance-based cash bonuses appropriately balance risk and the desire to focus our employees on specific short-term goals important to our success and do not encourage unnecessary or excessive risk taking.

A significant proportion of the compensation provided to our employees is in the form of long-term equity-based incentives that we believe are important to help further align our employees' interests with those of our stockholders. We do not believe that these equity-based incentives encourage unnecessary or excessive risk taking because their ultimate value is tied to our stock price.

Compensation Committee Interlocks and Insider Participation

During the fiscal year ended December 31, 2012, or for some portion thereof, Dr. Hoffman, Dr. Langer and Mr. Madden served as members of the compensation committee of our board of directors. No such person is currently, or has been at any time, one of our executive officers or employees. None of our executive officers currently serves, or has served during the last completed three fiscal years, as a member of the board of directors or compensation committee of any other entity that has or had one or more executive officers serving as a member of our board of directors or compensation committee.

Code of Business Conduct and Ethics

We have adopted a code of business conduct and ethics that applies to all of our employees, officers and directors, including those officers responsible for financial reporting. Following the completion of this offering, the code of business conduct and ethics will be available on our website at www.dicerna.com. We expect that any amendments to the code, or any waivers of its requirements, will be disclosed on our website.

Limitation of Liability and Indemnification

As permitted by the Delaware General Corporation Law, as amended, our certificate of incorporation and bylaws to be in effect at the completion of this offering will contain provisions that limit or eliminate the personal liability of our directors. Consequently, a director will not be personally liable to us or our stockholders for monetary damages for breach of fiduciary duty as a director, except for liability for:

n any breach of the director's duty of loyalty to us or our stockholders;

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- n any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- n any unlawful payments related to dividends or unlawful stock repurchases, redemptions or other distributions; or
- n any transaction from which the director derived an improper personal benefit.

These limitations of liability do not alter director liability under the U.S. federal securities laws and do not affect the availability of equitable remedies such as an injunction or rescission.

In addition, our bylaws provide that:

- n we will indemnify our directors, officers and, at the discretion of our board of directors, certain employees and agents to the fullest extent permitted by the Delaware General Corporation Law, as amended;
- n we will advance expenses, including attorneys' fees, to our directors and to our officers and certain employees, in connection with legal proceedings, subject to limited exceptions; and
- n any indemnification agreement we enter into with any individual director, officer, employee or agent shall supersede all of the indemnification rights conferred upon such person under our bylaws to the extent so provided in such indemnification agreement.

In connection with this offering, we will enter into indemnification agreements with each of our executive officers and directors. These agreements will provide that we will indemnify each of our executive officers and directors to the fullest extent permitted by law and advance expenses to each indemnitee in connection with any proceeding in which indemnification is available.

Prior to the completion of this offering, we expect to obtain general liability insurance that covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers, including liabilities under the Securities Act of 1933, as amended (Securities Act). Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling the registrant pursuant to the foregoing provisions, we have been informed that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

The above provisions may discourage stockholders from bringing a lawsuit against our directors for breach of their fiduciary duty. The provisions may also have the effect of reducing the likelihood of derivative litigation against directors and officers, even though such an action, if successful, might otherwise benefit us and our stockholders. Furthermore, a stockholder's investment may be adversely affected to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions. We believe that these provisions, the indemnification agreements and the insurance are necessary to attract and retain talented and experienced directors and officers.

At present, there is no pending litigation or proceeding involving any of our directors or officers where indemnification will be required or permitted. We are not aware of any threatened litigation or proceedings that might result in a claim for such indemnification.

Table of Contents**EXECUTIVE AND DIRECTOR COMPENSATION****Director Compensation Table Year Ended December 31, 2013**

The following table presents information regarding the compensation paid for 2013 to members of our board of directors who are not also employed by us or any of our subsidiaries (our non-employee directors). The compensation paid to Dr. Fambrough, who is also our chief executive officer, is presented below under Executive Compensation and the related explanatory tables. Dr. Fambrough is not entitled to receive additional compensation for his service as a director.

NAME	FEEES	OPTION	ALL OTHER	TOTAL
	EARNED OR PAID IN			
	CASH			
	(\$)	(\$)	(\$)	(\$)
Jonathan Fleming ⁽²⁾				
Brian K. Halak, Ph.D.				
Stephen J. Hoffman, M.D., Ph.D.				
James C. Jenson, Ph.D. ⁽³⁾	29,167	100,500		129,667
Peter Kolchinsky, Ph.D.				
Dennis Langer, M.D., J.D.	25,000	133,765		158,765
Jonathan MacQuitty, Ph.D. ⁽⁴⁾				
David M. Madden	75,000	225,167		300,167
Vincent J. Miles, Ph.D. ⁽⁵⁾				

⁽¹⁾ Pursuant to applicable Securities and Exchange Commission rules, the amounts reported in the Option Awards column of the table above reflect the fair value on the grant date of the option awards granted to our non-employee directors during 2013. These amounts also include an incremental charge for the repricing of certain stock options held by Dr. Langer and Mr. Madden during 2013. These values have been determined under the principles used to calculate the value of equity awards for purposes of our financial statements. For a discussion of the assumptions and methodologies used to calculate the amounts referred to above, please see the discussion of option awards contained in Note 10, Common Stock and Stock Option Plan, to our financial statements for the year ended December 31, 2012 and for the nine months ended September 30, 2013 included elsewhere in this prospectus. As of December 31, 2013, Dr. Jenson held outstanding options to purchase 50,000 shares of our common stock, Dr. Langer held outstanding options to purchase 50,900 shares of our common stock and Mr. Madden held outstanding options to purchase 112,511 shares of our common stock (in each case, after giving effect to the reverse split effected by us on July 25, 2013 as to options granted prior to that date). Other than these options, none of our non-employee directors held any outstanding options or other equity awards on that date.

⁽²⁾ Mr. Fleming resigned as a member of our board of directors in July 2013.

⁽³⁾ Dr. Jenson resigned as a member of our board of directors in July 2013.

⁽⁴⁾ Dr. MacQuitty resigned as a member of our board of directors in November 2013.

⁽⁵⁾ Dr. Miles joined our board of directors in November 2013.

Director Compensation

Prior to this offering, we did not have a formal policy for compensating our non-employee directors. However, non-employee directors who are not affiliated with any of our major stockholders may receive stock options and other equity awards under our stock incentive plans from time to time as determined by our board of directors. We also reimburse non-employee directors for travel expenses incurred in connection with their duties as directors. In addition, we entered into an offer letter with Mr. Madden, the chairman of our board of directors, in June 2009 that provides for him to receive an annual cash retainer of \$75,000 for his service as a director, and we entered into an offer letter with Dr. Langer in February 2011 that provides for him to receive an annual cash retainer of \$25,000 for his service as a director.

In 2009, we entered into a transition agreement with Dr. Jenson, our co-founder and former chief executive officer, to provide for the transition of his duties to a new chief executive officer. The agreement provided for Dr. Jenson to continue to serve as a member of our board of directors and to receive an annual retainer of \$50,000. In July 2013,

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we entered into an amendment of this agreement to provide for Dr. Jenson to serve on our scientific advisory board. Under the amendment, Dr. Jenson's annual retainer remains \$50,000, and we agreed not to terminate his service on the scientific advisory board at any time prior to December 31, 2013.

We expect to adopt a new compensation program for our non-employee directors following the consummation of this offering. We are still considering the design of this program and expect to retain an independent compensation consultant to help us determine its terms.

Executive Compensation

Overview

Our executive compensation program is based on a pay-for-performance philosophy. We designed our executive compensation program to achieve the following primary objectives:

- n provide compensation and benefit levels that will attract, retain, motivate and reward a highly talented executive team within the context of responsible cost management;
- n establish a direct link between our individual/team performance and results and our executives' compensation; and
- n align the interests and objectives of our executives with those of our stockholders by linking executive equity awards to stockholder value creation.

Compensation for our executive officers is comprised primarily of the following three main components.

- n *Base Salary.* Base salaries are determined on a case-by-case basis for each executive, including consideration of each officer's experience, expertise and performance, as well as market compensation levels for similar positions.
- n *Annual Cash Incentive Bonuses.* Annual cash incentive bonuses are contingent upon our achievement of certain operational and financial objectives, which for 2013 consisted primarily of research and development goals. Each executive's target bonus amount is expressed as a percentage of the executive's base salary and intended to be commensurate with the executive's position and responsibilities. Target bonuses for the executives ranged from 30 to 35 percent of base salary for the year ended December 31, 2013.
- n *Long-term Equity Incentives.* We believe equity awards in the form of options to purchase shares of our common stock provide an incentive for our executives to focus on driving growth in our stock price and long-term value creation and help us to attract and retain key talent. In addition, the granting of options helps ensure that the interests of our executive officers are aligned with those of our stockholders as the options only have value if the value of the Company's stock increases after the date the option is granted. In 2013, we granted options to our executives that would vest only if we achieved certain performance objectives deemed important to our success, as well as options that vest based on the executive's continued service to the Company and provide an additional retention incentive.

Our executive officers are entitled to certain benefits if the executive's employment terminates in certain circumstances or if a change of control occurs. We also may provide our executives with relocation, housing or other benefits in certain circumstances. However, we do not provide any of our executive officers with a tax gross-up payment on any severance or change-of-control benefits (although we may provide tax reimbursement payments on relocation and other benefits).

Our board of directors reviews (and, after this offering, our compensation committee will review) our executive officers' overall compensation packages on an annual basis or more frequently as it deems appropriate. From time to time, we may retain independent compensation consultants as we consider appropriate to help identify appropriate peer group companies and to obtain and evaluate current executive

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compensation data. We did not retain compensation consultants in designing our executive compensation programs for 2012 and 2013. However, we expect that the compensation committee will retain independent compensation consultants in connection with this offering.

Table of Contents**Summary Compensation Table**

The following table provides a summary of compensation paid to our principal executive officer and our two other most highly compensated executive officers for the year ended December 31, 2013 (collectively, the named executive officers).

Summary Compensation Table Year Ended December 31, 2013

NAME AND PRINCIPAL POSITION	FISCAL YEAR	BASE SALARY (\$)	BONUS (\$) ⁽²⁾	STOCK AWARDS (\$)	OPTION AWARDS (\$) ⁽¹⁾	NON-EQUITY INCENTIVE PLAN	ALL OTHER COMPENSATION	TOTAL (\$)
						COMPENSATION (\$) ⁽²⁾	(\$) ⁽³⁾	
Douglas M. Fambrough, III, Ph.D Chief Executive Officer	2013	375,000			1,151,485		8,875	1,535,360
	2012	375,000				65,625	8,688	449,313
James E. Dentzer ⁽⁴⁾ Chief Financial Officer	2013	20,401	45,000		882,813			948,214
Bob D. Brown, Ph.D Chief Scientific Officer, Senior Vice President	2013	315,000			445,778		78,654	839,432
	2012	315,000				47,250	73,108	435,358
James B. Weissman Chief Business Officer	2013	295,000			307,249		11,698	613,947
	2012	295,000			78,325	44,250	121,476	539,051

⁽¹⁾ Pursuant to applicable Securities and Exchange Commission rules, the amounts reported in the Option Awards column of the table above reflect the fair value on the grant date of the option awards granted to our named executive officers during 2013 and 2012, and do not reflect the actual amounts earned. These amounts also include an incremental charge for the repricing of certain stock options held by Dr. Fambrough, Dr. Brown and Mr. Weissman during 2013. These values have been determined under the principles used to calculate the value of equity awards for purposes of our financial statements. For a discussion of the assumptions and methodologies used to calculate the amounts referred to above, please see the discussion of option awards contained in Note 10, Common Stock and Stock Option Plan, to our financial statements for the year ended December 31, 2012 and for the nine months ended September 30, 2013 included elsewhere in this prospectus.

The amounts reported in this column for each executive for 2013 include certain grants of stock options that are subject to performance-based vesting requirements as described in the footnotes to the Outstanding Equity Awards at December 31, 2013 table below. These amounts are reported based on the probable outcome (as of the grant date) of the performance-based conditions applicable to the awards, as determined under generally accepted accounting principles. In each case, the amount was determined assuming that the maximum level of performance applicable to the award would be achieved.

⁽²⁾ These amounts include payments under our annual incentive bonus plan, which is based on our performance against certain operational and financial goals established by our compensation committee. Based on our overall performance against the performance objectives, our named executive officers were awarded bonuses of 50 percent of their target bonus levels for 2012. At the time of this filing, bonus amounts for 2013 had not yet been determined. When these amounts have been determined, we will disclose them in accordance with SEC rules. The amount reported in the Bonus column for Mr. Dentzer represents the first installment of a \$90,000 signing bonus provided under his employment agreement.

⁽³⁾ The amounts reported in this column consist of matching contributions we made to each executive's account under our 401(k) plan, as well as, in the case of Dr. Brown and Mr. Weissman, payment by us of certain temporary housing and relocation expenses and reimbursement for taxes incurred in connection with such payments.

⁽⁴⁾ Mr. Dentzer commenced employment with us in December 2013.

Employment Agreements

Douglas M. Fambrough, III, Ph.D.

In May 2010, we entered into an employment agreement with Dr. Fambrough to serve as our president and chief executive officer. Dr. Fambrough's employment with us is at-will, and the agreement does not include a specified term. The agreement provides that Dr. Fambrough receives an annual base salary, initially established at \$375,000, and that he is eligible for an annual incentive bonus, with his target bonus being 35 percent of his base salary. The board of directors will determine his actual bonus amount based on its assessment of the Company and individual performance during the year. The agreement also provides for Dr. Fambrough to participate in our benefit programs made available to our senior executives generally.

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Under Dr. Fambrough's agreement, if his employment is terminated by us without cause or by him for good reason (as such terms are defined in the agreement), he will be entitled to receive cash severance equal to twelve months of his base salary, reimbursement of his COBRA premiums for up to twelve months and a prorated payment of his target bonus for the year in which his termination occurs. If such a termination of Dr. Fambrough's employment occurs within one year after a change in control of the Company (as defined in the agreement), he would also be entitled to full acceleration of his stock options granted pursuant to the agreement. Dr. Fambrough's right to receive these severance benefits is subject to his providing a release of claims in favor of us.

James E. Dentzer

In November 2013, we entered into an employment agreement with Mr. Dentzer to serve as our chief financial officer beginning in December 2013. Mr. Dentzer's employment with us is at-will, and the agreement does not include a specified term. The agreement provides that Mr. Dentzer receives an annual base salary, initially established at \$335,000, and that he is eligible for an annual incentive bonus, with his target bonus being 35 percent of his base salary. The board of directors will determine his actual bonus amount based on its assessment of the Company and individual performance during the year. The agreement also provides for Mr. Dentzer to participate in our benefit programs made available to our senior executives generally.

Under Mr. Dentzer's agreement, if his employment is terminated by us without cause or by him for good reason (as such terms are defined in the agreement), he will be entitled to receive cash severance equal to six months of his base salary and reimbursement of his COBRA premiums for up to six months. If such a termination of Mr. Dentzer's employment occurs within one year after a change in control of the Company (as defined in the agreement), his cash severance would be equal to twelve months of his base salary and would be paid to him in a lump sum, and he would be eligible for reimbursement of his COBRA premiums for up to twelve months. Mr. Dentzer's right to receive these severance benefits is subject to his providing a release of claims in favor of us.

Bob D. Brown, Ph.D.

In May 2008, we entered into an employment agreement with Dr. Brown to serve as our senior vice president of research. Dr. Brown's employment with us is at-will, and the agreement does not include a specified term. The agreement provides that Dr. Brown receives an annual base salary, initially established at \$250,000, and that he is eligible for an annual incentive bonus, with his target bonus being 30 percent of his base salary. The board of directors will determine his actual bonus amount based on its assessment of the Company and individual performance during the year. The agreement also provides for Dr. Brown to participate in our benefit programs made available to our senior executives generally.

Under Dr. Brown's agreement, if his employment is terminated by us without cause or by him for good reason (as such terms are defined in the agreement), he will be entitled to receive cash severance equal to six months of his base salary and reimbursement of his COBRA premiums for up to six months. If such a termination of Dr. Brown's employment occurs within one year after a change in control of the Company (as defined in the agreement), his cash severance would be equal to twelve months of his base salary and would be paid to him in a lump sum, and he would be eligible for reimbursement of his COBRA premiums for up to twelve months. Dr. Brown's right to receive these severance benefits is subject to his providing a release of claims in favor of us.

James B. Weissman

In December 2011, we entered into an employment agreement with Mr. Weissman to serve as our chief business officer. Mr. Weissman's employment with us is at-will, and the agreement does not include a specified term. The agreement provides that Mr. Weissman receives an annual base salary, initially established at \$295,000, and that he is eligible for an annual incentive bonus, with his target bonus being 30 percent of his base salary. The board of directors will determine his actual bonus amount based on its assessment of the Company and individual performance during the year. The agreement also provides for Mr. Weissman to participate in our benefit programs made available to our senior executives generally.

Under Mr. Weissman's agreement, if his employment is terminated by us without cause or by him for good reason (as such terms are defined in the agreement), he will be entitled to receive cash severance equal to six months of his base salary and reimbursement of his COBRA premiums for up to six months. If such a termination of Mr. Weissman's employment occurs within one year after a change in control of the Company (as defined in the agreement), his cash severance would be equal to twelve months of his base salary and would be paid to him in a

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lump sum, and he would be eligible for reimbursement of his COBRA premiums for up to twelve months. Mr. Weissman's right to receive these severance benefits is subject to his providing a release of claims in favor of us.

The named executive officers' employment agreements also provide for grants of stock options by us as described in more detail in the Outstanding Equity Awards at December 31, 2013 table below and the footnotes that follow the table. The options granted to each executive officer under his employment agreement would generally vest on a change in control of the Company or, in Dr. Fambrough's case, an involuntary termination of his employment following a change in control. In January 2014, we entered into an agreement with Mr. Dentzer that provides for him to be reimbursed by us for any taxes imposed pursuant to Section 409A of the U.S. Internal Revenue Code of 1986, as amended, with respect to the option grant under his employment agreement. Each executive has also entered into an agreement that includes noncompetition and nonsolicitation covenants in favor of us that apply during the executive's employment with us and for two years thereafter.

Defined Contribution Plan

As part of our overall compensation program, we provide all full-time employees, including our named executive officers, with the opportunity to participate in a defined contribution 401(k) plan. Our 401(k) plan is intended to qualify under Section 401 of the Internal Revenue Code so that employee contributions and income earned on such contributions are not taxable to employees until withdrawn. Employees may elect to defer up to 96 percent of their eligible compensation (not to exceed the statutorily prescribed annual limit) in the form of elective deferral contributions to our 401(k) plan. Our 401(k) plan also has a catch-up contribution feature for employees aged 50 or older (including those who qualify as highly compensated employees) who can defer amounts over the statutory limit that applies to all other employees. We currently provide matching contributions under the plan of up to four percent of an employee's eligible compensation.

Table of Contents**Outstanding Equity Awards at December 31, 2013**

The following table presents information regarding the outstanding stock options held by each of the named executive officers as of December 31, 2013, including the vesting dates for the portions of these awards that had not vested as of that date. None of the named executive officers held any outstanding restricted stock or other equity awards as of that date.

NAME	GRANT DATE	NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS		EQUITY INCENTIVE PLAN AWARDS: NUMBER OF SECURITIES UNDERLYING UNEXERCISED UNEARNED OPTIONS		OPTION EXERCISE PRICE (\$)	OPTION EXPIRATION DATE
		EXERCISABLE (#)	UNEXERCISABLE (#)	UNEXERCISED (#)	UNEXERCISED (#)		
Douglas M. Fambrough, III, Ph.D.	6/8/10	300	750 ⁽¹⁾			3.42	6/8/20
	10/14/10	290	1,160 ⁽²⁾			3.42	10/14/20
	9/24/13	35,156	246,094 ⁽³⁾			3.42	9/23/23
	9/24/13				281,250 ⁽⁴⁾	3.42	9/23/23
James E. Dentzer	12/30/13		156,250 ⁽⁵⁾			3.42	12/30/23
Bob D. Brown, Ph.D.	5/7/08	1,200				3.42	5/7/18
	2/27/09	400				3.42	2/27/19
	10/14/10	1,333	267 ⁽⁶⁾			3.42	10/14/20
	9/24/13	16,406	114,844 ⁽³⁾			3.42	9/23/23
	9/24/13				87,500 ⁽⁷⁾	3.42	9/23/23
James B. Weissman	4/27/12	33	834 ⁽⁸⁾			3.42	4/26/22
	4/27/12				1,500 ⁽⁹⁾	3.42	4/26/22
	9/24/13	11,250	78,750 ⁽³⁾			3.42	9/23/23
	9/24/13				60,000 ⁽¹⁰⁾	3.42	9/23/23

(1) The unvested portion of this option vests in five monthly installments, with the last installment vesting on May 31, 2014.

(2) The unvested portion of this option vests in eight monthly installments, with the last installment vesting on August 5, 2014.

(3) These options vest in monthly installments, with the first such installment vesting July 30, 2013 and an additional installment vesting on the last day of each of the 47 months thereafter.

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- (4) This option vests based on the achievement of certain regulatory approvals, certain operational and business development goals and the listing of our common stock on the Nasdaq Stock Market, with 20 percent of the option vesting on the achievement of each such goal.
- (5) This option vests as to 25 percent of the option on December 9, 2014, and as to the remaining 75 percent of the option in 36 monthly installments thereafter.
- (6) This option vests as to 25 percent of the option on August 5, 2011, and as to the remaining 75 percent of the option in 36 monthly installments thereafter.
- (7) This option vests based on the achievement of certain regulatory approvals.
- (8) The unvested portion of this option vests in 25 monthly installments, with the last installment vesting on January 31, 2016.
- (9) This option vests based on the Company's deriving non-equity cash from new business development activity as set forth in Mr. Weissman's employment agreement.
- (10) This option vests 50 percent on the achievement of certain business development goals and 50 percent on the listing of our common stock on the Nasdaq Stock Market.

Equity Incentive Plans

As of December 31, 2013, our employees, directors and consultants hold outstanding stock options for the purchase of up to 1,621,678 shares of our common stock. Of these options, 5,950 were granted under our 2007 Employee, Director and Consultant Stock Plan, as amended (2007 Plan), and 1,615,728 were granted under our 2010 Employee, Director and Consultant Stock Plan, as amended (2010 Plan). As of December 31, 2013, 138,809 of

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those options were vested and the balance were not vested. The exercise price of each of those options was \$3.42 per share and each of those options had a maximum term of ten years from the applicable date of grant.

The following summaries provide more detailed information concerning our equity compensation plans. Each summary is qualified in its entirety by the full text of the applicable compensation plan and related form of award agreement, each of which has been filed with the Securities and Exchange Commission as an exhibit to the registration statement on Form S-1, of which this prospectus is a part, and is available through the website maintained by the Securities and Exchange Commission at <http://www.sec.gov>.

Prior plans

We adopted the 2007 Plan in July 2007, and stockholders approved the plan in July 2007. We adopted the 2010 Plan in October 2010, and stockholders approved the plan in October 2010. Our authority to grant new awards under the 2007 Plan terminated when we adopted the 2010 Plan. Under each of the 2007 Plan and the 2010 Plan (the Prior Plans), we are generally authorized to grant options to purchase shares of our common stock to employees, directors and consultants of us. Options under the Prior Plans are either incentive stock options, within the meaning of Section 422 of the Internal Revenue Code, or nonqualified stock options. All options granted under the Prior Plans expire no later than ten years from their date of grant. No new awards will be granted under the 2010 Plan after the consummation of this initial public offering.

Our board of directors, or a committee appointed by the board, administers the Prior Plans. As is customary in incentive plans of this nature, the number of shares subject to outstanding awards under the Prior Plans and the exercise prices of those awards are subject to adjustment in the event of changes in our capital structure, reorganizations and other extraordinary events. In the event that we are consolidated with or acquired by another entity in a merger, consolidation or sale of all or substantially all of our assets, the plan administrator will provide for the outstanding awards either to be assumed by our successor or to terminate on the transaction. If the awards terminate, the plan administrator has discretion to provide for the accelerated vesting of the awards prior to their termination.

Our board of directors may amend or terminate the Prior Plans at any time, except that any such amendment or termination may not adversely affect the rights of a holder of an outstanding award without the holder's consent. The Prior Plans require that certain amendments, to the extent required by applicable law or any applicable listing agency or deemed necessary or advisable by the board of directors, be submitted to stockholders for their approval.

2014 Performance Incentive Plan

Our board of directors and stockholders have approved the adoption of a 2014 Performance Incentive Plan (2014 Plan), which will become effective immediately prior to the consummation of this offering. The 2014 Plan will provide an additional means through the grant of awards to attract, motivate, retain and reward selected employees and other eligible persons. Employees, officers, directors and consultants that provide services to us may be selected to receive awards under the 2014 Plan.

Our board of directors, or one or more committees appointed by the board or another committee (within delegated authority), will administer the 2014 Plan. The administrator of the plan has broad authority:

- n to select participants and determine the types of awards they are to receive;
- n to determine the number of shares subject to awards and the terms and conditions of awards, including any price to be paid for the shares or the award and to establish any vesting conditions of such shares or awards;
- n to cancel, modify or waive our rights with respect to, or modify, discontinue, suspend or terminate any or all outstanding awards, subject to any required consents;
- n to construe and interpret the terms of the 2014 Plan and any agreements relating to the 2014 Plan;

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- n to accelerate or extend the vesting or exercisability or extend the term of any or all outstanding awards subject to any required consent;

- n subject to the other provisions of the 2014 Plan, to make certain adjustments to an outstanding award and authorize the termination, conversion, substitution or succession of an award; and

- n to allow the purchase price of an award or shares of our common stock to be paid in the form of cash, check or electronic funds transfer, by the delivery of previously-owned shares of our common stock or by a

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reduction of the number of shares deliverable pursuant to the award, by services rendered by the recipient of the award, by notice and third party payment or cashless exercise on such terms as the administrator may authorize or any other form permitted by law.

A total of 1,900,000 shares of our common stock will be authorized for issuance with respect to awards granted under the 2014 Plan. The share limit will automatically increase on the first trading day in January of each year (commencing with January 2015) by an amount equal to the lesser of (1) four percent of the total number of outstanding shares of our common stock on the last trading day in December in the prior year and (2) such lesser number as determined by our board of directors. In addition, a maximum of 10,000,000 shares of common stock may be delivered pursuant to incentive stock options under the 2014 Plan, and the maximum number of shares that may be subject to options and stock appreciation rights granted to any one individual in a calendar year is 2,000,000 shares. Any shares subject to awards that are not paid, delivered or exercised before they expire, are canceled or terminated or that fail to vest, as well as shares used to pay the purchase or exercise price of awards or related tax withholding obligations, will become available for other award grants under the 2014 Plan. As of the date of this prospectus, no awards have been granted under the 2014 Plan, and the full number of shares authorized under the 2014 Plan is available for award purposes.

Awards under the 2014 Plan may be in the form of incentive or nonqualified stock options, stock appreciation rights, stock bonuses, restricted stock, stock units and other forms of awards, including cash awards. Awards under the plan generally will not be transferable other than by will or the laws of descent and distribution, except that the plan administrator may authorize certain transfers.

Nonqualified and incentive stock options may not be granted at prices below the fair market value of the common stock on the date of grant. Incentive stock options must have an exercise price that is at least equal to the fair market value of our common stock, or 110 percent of fair market value of our common stock or incentive stock option grants to any ten percent owner of our common stock, on the date of grant. These and other awards may also be issued solely or in part for services. Awards are generally paid in cash or shares of our common stock. The plan administrator may provide for the deferred payment of awards and may determine the terms applicable to deferrals.

As is customary in incentive plans of this nature, the number and type of shares available under the 2014 Plan and any outstanding awards, as well as the exercise or purchase price of awards, will be subject to adjustment in the event of certain reorganizations, mergers, combinations, recapitalizations, stock splits, stock dividends or other similar events that change the number or kind of shares outstanding and extraordinary dividends or distributions of property to the stockholders. In no case (except due to an adjustment referred to above or any repricing that may be approved by our stockholders) will any adjustment be made to a stock option or stock appreciation right award under the 2014 Plan (by amendment, cancellation and regrant, exchange or other means) that would constitute a repricing of the per-share exercise or base price of the award.

Generally, and subject to limited exceptions set forth in the 2014 Plan, if we dissolve or undergo certain corporate transactions such as a merger, business combination or other reorganization, or a sale of all or substantially all of its assets, all awards then-outstanding under the 2014 Plan will become fully vested or paid, as applicable, and will terminate or be terminated in such circumstances, unless the plan administrator provides for the assumption, substitution or other continuation of the award. The plan administrator also has the discretion to establish other change in control provisions with respect to awards granted under the 2014 Plan. For example, the administrator could provide for the acceleration of vesting or payment of an award in connection with a corporate event that is not described above and provide that any such acceleration shall be automatic upon the occurrence of any such event.

Our board of directors may amend or terminate the 2014 Plan at any time, but no such action will affect any outstanding award in any manner materially adverse to a participant without the consent of the participant. Plan amendments will be submitted to stockholders for their approval as required by applicable law or any applicable listing agency. The 2014 Plan is not exclusive, and our board of directors and compensation committee may grant stock and performance incentives or other compensation, in stock or cash, under other plans or authority.

The plan will terminate in January 2024. However, the plan administrator will retain its authority until all outstanding awards are exercised or terminated. The maximum term of options, stock appreciation rights and other rights to acquire common stock under the plan is ten years after the initial date of the award.

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2014 Employee Stock Purchase Plan

Our board of directors and stockholders have approved the adoption of a 2014 Employee Stock Purchase Plan (Purchase Plan), which will become effectively immediately prior to the consummation of this offering. The Purchase Plan will provide an additional means to attract, motivate, retain and reward employees and other eligible persons by allowing them to purchase additional shares of our common stock.

The Purchase Plan is designed to allow our eligible employees and the eligible employees of our participating subsidiaries to purchase shares of our common stock, at semi-annual intervals, with their accumulated payroll deductions.

Share Reserve

A total of 1,000,000 shares of our common stock will initially be available for issuance under the Purchase Plan. The share limit will automatically increase on the first trading day in January of each year (commencing with January 2015) by an amount equal to the lesser of (1) one percent of the total number of outstanding shares of our common stock on the last trading day in December in the prior year, (2) 1,000,000 shares and (3) such lesser number as determined by our board of directors.

Offering Periods

The Purchase Plan will have a series of successive overlapping offering periods with a new offering period beginning on the first business day of January and July each year and continuing for a period of 24 months. However, the initial offering period will begin on the first business day of April 2014 and will last for 21 months. Each offering period will consist of four purchase periods, each with a six-month duration (or three months for the purchase period that begins in April 2014). Purchase periods will commence on the first business day of January and July and will end on the last business day of the immediately following June or December, respectively.

Eligible Employees. Individuals scheduled to work more than 20 hours per week for more than five calendar months per year may join an offering period on the start date of that period. Employees may participate in only one offering period at a time.

Payroll Deductions

A participant may contribute up to 15 percent of his or her cash earnings through payroll deductions, and the accumulated deductions will be applied to the purchase of shares on each semi-annual purchase date. Unless otherwise provided in advance by the administrator, the purchase price per share will be equal to 85 percent of the fair market value per share on the start date of the offering period or, if lower, 85 percent of the fair market value per share on the semi-annual purchase date. In no event, however, may any participant purchase more than 10,000 shares on any purchase date.

Reset Feature

If the fair market value per share of our common stock on any purchase date is less than the fair market value per share on the start date of the two-year offering period, then that offering period will automatically terminate and participants in that offering period will automatically be enrolled in the new 24-month offering period beginning on the next business day.

Change in Control

If we are acquired by merger or sale of all or substantially all of our assets or more than 50 percent of our voting securities, then all outstanding purchase rights will automatically be exercised on or prior to the effective date of the acquisition, unless the plan administrator provides for the rights to be settled in cash or exchanged or substituted on the transaction. Unless otherwise provided in advance by the plan administrator, the purchase price will be equal to 85 percent of the market value per share on the start date of the offering period in which the acquisition occurs or, if lower, 85 percent of the fair market value per share on the purchase date.

Other Plan Provisions

No new offering periods will commence after January 2034. The board of directors may at any time amend, suspend or discontinue the Purchase Plan. However, certain amendments may require stockholder approval.

Table of Contents**CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS**

Below we describe transactions and series of related transactions to which we were a party, or may be a party in relation to this offering, and which we have entered since January 1, 2010, in which:

- n the amounts involved exceeded or will exceed \$120,000; and
- n any of our directors, executive officers or holders of more than five percent of our capital stock, or an affiliate or immediate family member thereof, had or will have a direct or indirect material interest.

Participation in this Offering

Certain of our existing stockholders, including affiliates of our directors, have agreed to purchase an aggregate of 3,400,000 shares of our common stock in this offering at the initial public offering price.

Issuance of Convertible Promissory Notes and Warrants*Issuance of convertible promissory notes and warrants in 2013*

In June 2013, we issued convertible promissory notes in an aggregate principal amount of \$3.0 million. Each convertible promissory note bore a simple interest rate of seven percent per annum. The aggregate principal amount of the convertible promissory notes converted into an aggregate of 428,526 shares of our Series C preferred stock on July 30, 2013. We paid the accrued interest through July 30, 2013 in cash. We issued seven warrants to purchase our Series C preferred stock to the purchasers of the convertible promissory notes in connection with the issuance thereof for an aggregate warrant purchase price of \$300. See *Description of Capital Stock Warrants* for a description of the warrants. The following table sets forth the loan amounts provided by our directors, executive officers and holders of more than five percent of our capital stock, or an affiliate or immediate family member thereof, and the number of shares of our Series C preferred stock issuable upon exercise of the warrants held by such persons.

NAME	LOAN AMOUNT	NUMBER OF SHARES OF SERIES C PREFERRED STOCK ISSUABLE UPON EXERCISE OF WARRANT
Skyline Venture Partners V, L.P.	\$ 759,409.05	21,697
Entities affiliated with Domain Associates ⁽¹⁾	\$ 741,908.80	21,197
Entities affiliated with Oxford Biosciences Partners V, L.P. ⁽²⁾	\$ 715,597.43	20,445
Abingworth Bioventures V, LP	\$ 535,481.45	15,299
S.R. One, Limited	\$ 247,303.27	7,065

⁽¹⁾ Consists of (a) a loan amount of \$736,444.35 provided by Domain Partners VIII, L.P., (b) a loan amount of \$5,464.45 provided by DP VIII Associates, L.P., (c) 21,041 shares of our Series C preferred stock issuable upon exercise of the warrant held by Domain Partners VIII, L.P. and (d) 156 shares of our Series C preferred stock issuable upon exercise of the warrant held by DP VIII Associates, L.P.

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- ⁽²⁾ Consists of (a) a loan amount of \$699,827.01 provided by Oxford Bioscience Partners V, L.P., (b) a loan amount of \$15,770.42 provided by mRNA Fund V L.P., (c) 19,995 shares of our Series C preferred stock issuable upon exercise of the warrant held by Oxford Bioscience Partners V, L.P. and (d) 450 shares of our Series C preferred stock issuable upon exercise of the warrant held by mRNA Fund V L.P.

Table of Contents***Issuance of convertible promissory notes and warrants in 2010***

In June and July 2010, we issued convertible promissory notes in an aggregate principal amount of \$5.5 million. Each convertible promissory note bore a simple interest rate of seven percent per annum. The aggregate principal amount and accrued interest of the convertible promissory notes converted into an aggregate of 222,023 shares of our Series B preferred stock (after giving effect to the reverse stock split effected by us on July 25, 2013) on August 5, 2010. We issued five warrants to purchase shares of our common stock to the holders of the convertible promissory notes in connection with the issuance thereof. See Description of Capital Stock Warrants for a description of the warrants. The following table sets forth the loan amounts provided by our directors, executive officers and holders of more than five percent of our capital stock, or an affiliate or immediate family member thereof, and the number of shares of our common stock issuable upon exercise of the warrants held by such persons (after giving effect to the reverse stock split effected by us on July 25, 2013).

NAME	LOAN AMOUNT	NUMBER OF SHARES OF COMMON STOCK ISSUABLE UPON EXERCISE OF WARRANT
Skyline Venture Partners V, L.P.	\$ 1,888,619.85	755
Entities affiliated with Oxford Biosciences Partners V, L.P. ⁽¹⁾	\$ 1,779,661.00	711
Abingworth Bioventures V, LP	\$ 1,331,719.13	532

⁽¹⁾ Consists of (a) a loan amount of \$1,740,440.00 provided by Oxford Bioscience Partners V, L.P., (b) a loan amount of \$39,221.00 provided by mRNA Fund V L.P., (c) 696 shares of our common stock issuable upon exercise of the warrant held by Oxford Bioscience Partners V, L.P. and (d) 15 shares of our common stock issuable upon exercise of the warrant held by mRNA Fund V L.P.

Issuances of Preferred Stock***Issuance of Series C preferred stock***

In July 2013, we issued and sold 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 purchase price of approximately \$60.0 million in cash and pursuant to the conversion of previously outstanding convertible promissory notes, including the notes described above in Issuances of convertible promissory notes and warrants Issuance of convertible promissory notes and warrants in 2013 . The following table sets forth the number of shares of Series C preferred stock issued to our directors, executive officers and holders of more than five percent of our capital stock, or an affiliate or immediate family member thereof.

NAME	NUMBER OF SHARES OF SERIES C PREFERRED STOCK	AGGREGATE PURCHASE PRICE
RA Capital Healthcare Fund, LP	1,428,571	\$ 9,999,997.00
Affiliates of Deerfield Mgmt, L.P. ⁽¹⁾	1,428,569	\$ 9,999,983.00
Entities affiliated with Domain Associates ⁽²⁾	1,285,712	\$ 8,999,990.80
Skyline Venture Partners V, L.P.	1,043,429	\$ 7,304,003.05
Brookside Capital Partners Fund LP	1,000,000	\$ 7,000,000.00
Abingworth Bioventures V, LP	735,751	\$ 5,150,259.45

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S.R. One, Limited	678,151	\$	4,747,057.27
Entities affiliated with Oxford Biosciences Partners V, L.P. ⁽³⁾	285,712	\$	1,999,992.43
Dennis H. Langer, M.D., J.D. ⁽⁴⁾	71,428	\$	499,996.00

⁽¹⁾ Consists of (a) 499,285 shares purchased by Deerfield Private Design Fund II, L.P., (b) 572,142 shares purchased by Deerfield Private Design International II, L.P., (c) 161,071 shares purchased by Deerfield Special Situations Fund International Master Fund, L.P. and (d) 196,071 shares purchased by Deerfield Special Situations Fund, L.P.

⁽²⁾ Consists of (a) 1,276,243 shares purchased by Domain Partners VIII, L.P. and (b) 9,469 shares purchased by DP VIII Associates, L.P.

⁽³⁾ Consists of (a) 279,417 shares purchased by Oxford Bioscience Partners V, L.P. and (b) 6,295 shares purchased by mRNA Fund V L.P.

⁽⁴⁾ Purchased by Langer Family Holdings, LLLP. Dennis H. Langer, M.D., J.D. is a manager of Langer Family Investments, LLC, which is the general partner of Langer Family Holdings, LLLP. Dr. Langer disclaims beneficial ownership of the shares owned by Langer Family Holdings, LLLP.

Table of Contents**Issuance of Series B preferred stock**

In August, September and October 2010, we issued and sold an aggregate of 1,162,021 shares of our Series B preferred stock at a purchase price of \$25.00 per share (after giving effect to the reverse stock split effected by us as of July 25, 2013), for an aggregate purchase price of approximately \$29.0 million in cash and pursuant to the conversion of certain previously outstanding convertible promissory notes, including the notes described above in Issuances of convertible promissory notes and warrants Issuance of convertible promissory notes and warrants in 2010 . The following table sets forth the number of shares of Series B preferred stock (after giving effect to the reverse stock split effected by us as of July 25, 2013) issued to our directors, executive officers and holders of more than five percent of our capital stock, or an affiliate or immediate family member thereof.

NAME	NUMBER OF SHARES OF SERIES B PREFERRED STOCK	AGGREGATE PURCHASE PRICE
Entities affiliated with Domain Associates ⁽¹⁾	479,999	\$ 12,000,000
Skyline Venture Partners V, L.P.	179,322	\$ 4,483,062
Entities affiliated with Oxford Biosciences Partners V, L.P. ⁽²⁾	168,976	\$ 4,224,425
S.R. One, Limited	160,000	\$ 4,000,000
Abingworth Bioventures V, LP	126,445	\$ 3,161,135
Dennis H. Langer, M.D., J.D. ⁽³⁾	8,586	\$ 214,661
Roberto Guerciolini, M.D. ⁽⁴⁾	8,586	\$ 214,661

⁽¹⁾ Consists of (a) 476,464 purchased by Domain Partners VIII, L.P. and (b) 3,535 shares purchased by DP VIII Associates, L.P.

⁽²⁾ Consists of (a) 165,253 shares purchased by Oxford Bioscience Partners V, L.P. and (b) 3,723 shares purchased by mRNA Fund V L.P.

⁽³⁾ Purchased by Langer Family Holdings, LLLP. Dennis H. Langer, M.D., J.D. is a manager of Langer Family Investments, LLC, which is the general partner of Langer Family Holdings, LLLP. Dr. Langer disclaims beneficial ownership of the shares owned by Langer Family Holdings, LLLP.

⁽⁴⁾ Roberto Guerciolini, M.D., was our former senior vice president of pharmaceutical development.

Registration Rights Agreement

We have entered into an amended and restated registration rights agreement that provides holders of our preferred stock, including holders of five percent or more of our capital stock and entities affiliated with certain of our directors, with certain registration rights, including the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing under certain circumstances. These holders have waived their right to include shares in the registration statement of which this prospectus forms a part. See Description of Capital Stock Registration rights for more information about the registration rights.

Stockholders Agreement

We have entered into an amended and restated stockholders agreement under which certain holders of our capital stock, including certain holders of five percent or more of our capital stock and entities affiliated with certain of our directors, have agreed to vote in a certain way on certain matters, including with respect to the election of directors. Upon the closing of this offering, the voting agreement will terminate and none of our stockholders will have any special rights regarding the election or designation of members of our board of directors.

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The amended and restated stockholders agreement also provides for rights of first offer in favor of the holders of our preferred stock with respect to certain issuances of our capital stock and securities convertible into or exercisable or exchangeable for our capital stock. The stockholders agreement also provides for rights of first refusal and co-sale with respect to the shares of our common stock held by certain key holders of our common stock. The rights of first offer and the rights of first refusal and co-sale will terminate upon the closing of this offering.

Director and Executive Officer Compensation

See Executive and Director Compensation for information regarding compensation of our directors and named executive officers.

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Employment Agreements

We have entered into employment agreements with Douglas M. Fambrough, III, Ph.D., James E. Dentzer, Bob D. Brown, Ph.D. and James B. Weissman, our chief executive officer, chief financial officer, chief scientific officer and chief business officer, respectively. See [Executive and Director Compensation Employment Agreements](#) and [Executive and Director Compensation Termination-Based Compensation](#) for more information regarding each of these employment agreements. In addition, we entered into an agreement with Mr. Dentzer in January 2014, which provides for him to be reimbursed by us for any taxes imposed pursuant to Section 409A of the U.S. Internal Revenue Code of 1986, as amended, with respect to the option grant under his employment agreement.

Consulting Agreement

In June 2010, we entered into a consulting agreement with David Cordo, who served as our chief financial officer until December 2013, pursuant to which Mr. Cordo performed chief financial officer services to us for up to 20 hours per week. The consulting agreement provided for a service fee of \$200 per hour and reimbursement of out-of-pocket and travel expenses incurred in the provision of the services. We granted Mr. Cordo stock options to purchase a total of 12,780 shares of our common stock in 2008, 2010 and 2013 under our stock incentive plans.

Non-employee Director Agreements

We entered into letter agreements with David M. Madden and Dennis H. Langer, M.D., J.D., two of our non-employee directors, in June 2009 and February 2011, respectively. See [Executive and Director Compensation Director Compensation](#) for more information regarding these agreements.

Transition and Separation Agreements

In 2009, we entered into a transition agreement with Dr. Jenson, our co-founder and former chief executive officer, to provide for the transition of his duties to a new chief executive officer. The agreement provided for Dr. Jenson to continue to serve as a member of our board of directors and to receive an annual retainer of \$50,000. In July 2013, we entered into an amendment of this agreement to provide for Dr. Jenson to serve on our scientific advisory board. Under the amendment, Dr. Jenson's annual retainer remains \$50,000, and we agreed not to terminate his service on the scientific advisory board at any time prior to December 31, 2013.

Indemnification Agreements and Directors and Officers Liability Insurance

We have entered into indemnification agreements with each of our directors and executive officers. These agreements, among other things, require us or will require us to indemnify each director (and in certain cases their affiliated venture capital funds) and executive officer to the fullest extent permitted by Delaware law, including indemnification of expenses such as attorneys' fees, judgments, fines and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action or proceeding by or in right of us, arising out of the person's services as a director or executive officer.

Policies and Procedures for Related Party Transactions

We have adopted a written related person transaction policy, which will become effective immediately prior to the completion of this offering and will set forth the policies and procedures for the review and approval or ratification of related person transactions. This policy will cover, with certain exceptions set forth in Item 404 of Regulation S-K promulgated under the Exchange Act, any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we were or are to be a participant, where the amount involved exceeds \$120,000 and a related person had, has or will have a direct or indirect material interest, including purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related person. As provided by our audit committee charter, our audit committee will be responsible for reviewing and approving in advance the related party transactions covered by our related transaction policies and procedures.

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PRINCIPAL STOCKHOLDERS

The following table sets forth certain information relating to the beneficial ownership of our common stock as of December 31, 2013, by:

- n each person, or group of affiliated persons, known by us to beneficially own more than five percent of the outstanding shares of our common stock;

- n each of our directors;

- n each of our named executive officers; and

- n all directors and executive officers as a group.

The number of shares beneficially owned by each entity, person, director or executive officer is determined in accordance with the rules of the Securities and Exchange Commission, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or dispositive power as well as any shares that the individual has the right to acquire within 60 days of December 31, 2013 through the exercise of any stock option, warrants or other rights. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and dispositive power with respect to all shares of common stock held by that person.

The percentage of shares beneficially owned prior to this offering is computed on the basis of 10,627,660 shares of our common stock outstanding as of December 31, 2013, which reflects the assumed conversion of all of the outstanding shares of our preferred stock into an aggregate of 10,589,434 shares of common stock immediately upon the closing of this offering, as if the conversion had occurred as of December 31, 2013. The percentage of shares beneficially owned after this offering is computed on the basis of 16,627,660 shares of common stock outstanding immediately after the closing of this offering (assuming no exercise of the underwriters' over-allotment option to purchase additional shares of our common stock). Shares of our common stock that a person has the right to acquire within 60 days of December 31, 2013 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all directors and executive officers as a group. Unless otherwise noted below, the address of the persons listed on the table is c/o Dicerna Pharmaceuticals, Inc., 480 Arsenal Street, Building 1, Suite 120, Watertown, MA 02472.

Certain of our existing stockholders, including affiliates of our directors, have agreed to purchase an aggregate of 3,400,000 shares of our common stock in this offering at the initial public offering price. The following table reflects such purchase in the calculation of the number of shares beneficially owned after the offering and the calculation of the percentage of shares beneficially owned after the offering. The calculation of the percentage of shares beneficially owned after the offering assumes no exercise of the underwriters' option to purchase additional shares.

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NAME AND ADDRESS OF BENEFICIAL OWNER	SHARES OF COMMON STOCK BENEFICIALLY OWNED		PERCENTAGE OF SHARES BENEFICIALLY OWNED	
	BEFORE OFFERING	AFTER OFFERING	BEFORE OFFERING	AFTER OFFERING
5 percent or Greater Stockholders				
Entities affiliated with Domain Associates ⁽¹⁾	1,786,908	1,786,908	16.8%	10.7%
Skyline Venture Partners V, L.P. ⁽²⁾	1,557,203	1,757,203	14.7%	10.6%
Affiliates of Deerfield Mgmt, L.P. ⁽³⁾	1,428,569	2,428,569	13.4%	14.6%
RA Capital Healthcare Fund, LP ⁽⁴⁾	1,428,571	2,428,571	13.4%	14.6%
Abingworth Bioventures V, LP ⁽⁵⁾	1,098,027	1,198,027	10.3%	7.2%
Brookside Capital Partners Fund LP ⁽⁶⁾	1,000,000	2,000,000	9.4%	12.0%
S.R. One, Limited ⁽⁷⁾	845,216	845,216	8.0%	5.1%
Entities affiliated with Oxford Biosciences Partners V, L.P. ⁽⁸⁾	771,838	771,838	7.3%	4.6%
Directors and Named Executive Officers				
Douglas M. Fambrough, III, Ph.D. ⁽⁹⁾	117,925	117,925	1.1%	*
Brian K. Halak, Ph.D. ⁽¹⁰⁾	1,786,908	1,786,908	16.8%	10.7%
Stephen J. Hoffman, M.D., Ph.D. ⁽¹¹⁾	1,557,203	1,757,203	14.7%	10.6%
Peter Kolchinsky, Ph.D. ⁽¹²⁾	1,428,571	2,428,571	13.4%	14.6%
Dennis H. Langer, M.D., J.D. ⁽¹³⁾	107,205	107,205	1.0%	*
David M. Madden ⁽¹⁴⁾	26,955	26,955	*	*
Vincent J. Miles, Ph.D. ⁽¹⁵⁾	1,098,027	1,198,027	10.3%	7.2%
James E. Dentzer				
Bob D. Brown, Ph.D. ⁽¹⁶⁾	25,075	25,075	*	*
James B. Weissman ⁽¹⁷⁾	15,966	15,966	*	*
All directors and executive officers as a group (10 persons) ⁽¹⁸⁾	6,163,835	7,463,835	58.0%	44.9%

* Indicates beneficial ownership of less than one percent of the outstanding shares of our common stock.

(1) Consists of (a) 476,464 shares of common stock issuable upon conversion of shares of Series B preferred stock held by Domain Partners VIII, L.P. (Domain Partners), (b) 1,276,243 shares of common stock issuable upon conversion of shares of Series C preferred stock held by Domain Partners, (c) 21,041 shares of common stock issuable upon conversion of Series C preferred stock issuable upon exercise of a preferred stock warrant held by Domain Partners that is exercisable as of December 31, 2013 or will become exercisable within 60 days of such date, (d) 3,535 shares of common stock issuable upon conversion of Series B preferred stock held by DP VIII Associates, L.P. (DP Associates), (e) 9,469 shares of common stock issuable upon conversion of Series C preferred stock held by DP Associates and (f) 156 shares of common stock issuable upon conversion of Series C preferred stock issuable upon exercise of a preferred stock warrant held by DP Associates that is exercisable as of December 31, 2013 or will become exercisable within 60 days of such date. James C. Blair, Brian H. Dovey, Jesse I. Treu, Kathleen K. Schoemaker, Brian K. Halak and Nicole Vitullo, the managing members of One Palmer Square Associates VIII, L.L.C., the general partner of Domain Partners and DP Associates, share the power to vote or dispose of the shares held by of Domain Partners and DP Associates and therefore each of the foregoing managing members may be deemed to have voting and dispositive power with respect to such shares. Each of the foregoing managing members disclaims beneficial ownership of such shares except to the extent of his or her pecuniary interest therein, if any. Brian K. Halak, Ph.D. is a member of our board of directors. The address of Domain Partners and DP Associates is One Palmer Square, Suite 515, Princeton, NJ 08542.

(2) Consists of (a) 312,000 shares of common stock issuable upon conversion of shares of Series A preferred stock, (b) 179,322 shares of common stock issuable upon conversion of shares of Series B preferred stock, (c) 1,043,429 shares of common stock issuable upon conversion of Series C preferred stock, (d) 755 shares of common stock issuable upon exercise of a common stock warrant that is exercisable as of December 31, 2013 or will become exercisable within 60 days of such date and (e) 21,697 shares of common stock issuable upon conversion of shares of Series C preferred stock issuable upon exercise of a preferred stock warrant that is exercisable as of December 31, 2013 or will become exercisable within 60 days of such date. All of the shares of preferred stock and warrants are held by Skyline Venture Partners V, L.P. John G. Freund, M.D. and Yasunori Kaneko, M.D. are Managing Directors of Skyline Venture Management V, LLC, the general partner of Skyline Venture Partners V, L.P., and may be deemed to share voting and dispositive power over the shares held by Skyline Venture Partners V, L.P. Stephen Hoffman, M.D., Ph.D., a member of our board of directors, is a member of Skyline Venture Management V,

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LLC and may be deemed to share voting and dispositive power over the shares held by Skyline Venture Partners V, L.P. Each of Drs. Freund, Kaneko and Hoffman disclaims beneficial ownership of such shares, except to the extent of his pecuniary interest therein. The address of Skyline Ventures Partners V, L.P. is 525 University Avenue, Suite 610, Palo Alto, CA 94301. The number of shares beneficially owned after the offering and the percentage of shares beneficially owned after the offering also include 200,000 shares that Skyline Venture Partners V, L.P. or its affiliated entities have agreed to purchase in the offering.

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- (3) Consists of (a) 499,285 shares of common stock issuable upon conversion of shares of Series C preferred stock held by Deerfield Private Design Fund II, L.P., (b) 572,142 shares of common stock issuable upon conversion of shares of Series C preferred stock held by Deerfield Private Design International II, L.P., (c) 161,071 shares of common stock issuable upon conversion of shares of Series C preferred stock held by Deerfield Special Situations Fund International Master Fund, L.P. and (d) 196,071 shares of common stock issuable upon conversion of shares of Series C preferred stock held by Deerfield Special Situations Fund, L.P. (collectively, the Deerfield Funds). Deerfield Mgmt, L.P. is the general partner of each of the Deerfield Funds. Deerfield Management Company, L.P. is the investment manager of each of the Deerfield Funds. Mr. James E. Flynn is the sole member of the general partner of each of Deerfield Mgmt, L.P. and Deerfield Management Company, L.P. Each of Deerfield Mgmt, L.P., Deerfield Management Company, L.P. and Mr. Flynn may be deemed to beneficially own the shares held by the Deerfield Funds. The address of Deerfield Funds is 780 Third Avenue, 37th Floor, New York, NY 10017. The number of shares beneficially owned after the offering and the percentage of shares beneficially owned after the offering also include 1,000,000 shares that the Deerfield Funds or their affiliated entities have agreed to purchase in the offering.
- (4) Consists of 1,428,571 shares of common stock issuable upon conversion of shares of Series C preferred stock held by RA Capital Healthcare Fund, LP. RA Capital Management, LLC is the sole general partner of the RA Capital Healthcare Fund, LP. Peter Kolchinsky, Ph.D., a member of our board of directors, is the manager of RA Capital Management, LLC. Each of Dr. Kolchinsky and RA Capital Management, LLC may be deemed to beneficially own the shares held by RA Capital Healthcare Fund, LP. Each of them disclaims beneficial ownership of such shares, except to the extent of its or his respective pecuniary interest therein. The address of RA Capital Healthcare Fund, LP is c/o RA Capital Management, LLC, 20 Park Plaza, Suite 1200, Boston, MA 02116. The number of shares beneficially owned after the offering and the percentage of shares beneficially owned after the offering also include 1,000,000 shares that RA Capital Management, LLC or its affiliated entities have agreed to purchase in the offering.
- (5) Consists of (a) 220,000 shares of common stock issuable upon conversion of shares of Series A preferred stock, (b) 126,445 shares of common stock issuable upon conversion of shares of Series B preferred stock, (c) 735,751 shares of common stock issuable upon conversion of shares of Series C preferred stock, (d) 532 shares of common stock issuable upon exercise of a common stock warrant that is exercisable as of December 31, 2013 or will become exercisable within 60 days of such date and (e) 15,299 shares of common stock issuable upon conversion of shares of Series C preferred stock issuable upon exercise of a preferred stock warrant that is exercisable as of December 31, 2013 or will become exercisable within 60 days of such date. All of the shares of preferred stock and warrants are held by Abingworth Bioventures V, LP. Abingworth LLP is the manager of Abingworth Bioventures V, LP and may be deemed to beneficially own the shares held by Abingworth Bioventures V, LP. An investment committee, comprised of Joseph Anderson, Jonathan M. MacQuitty, Michael F. Bigham and Stephen W. Bunting, approves investment and voting decisions by a majority vote, and no individual member has the sole control or voting power over the shares held by Abingworth Bioventures V, LP. Each of Abingworth LLP, Joseph Anderson, Jonathan M. MacQuitty, Michael F. Bigham and Stephen W. Bunting disclaims the beneficial ownership of such shares, except to the extent of its or his pecuniary interest therein. The address of Abingworth Bioventures V, LP is 38 Jermyn Street, London SW1Y 6DN, United Kingdom. The number of shares beneficially owned after the offering and the percentage of shares beneficially owned after the offering also include 100,000 shares that Abingworth LLP or its affiliated entities have agreed to purchase in the offering.
- (6) Consists of 1,000,000 shares of common stock issuable upon conversion of shares of Series C preferred stock. Brookside Capital Management, LLC is the general partner of Brookside Capital Investors, L.P., which is the general partner of Brookside Capital Partners Fund LP. Brookside Capital Management, LLC is controlled by an executive committee whose members include Dewey J. Awad, Domenic J. Ferrante, Matthew V. McPherron, William E. Pappendick IV and John M. Toussaint, who may be deemed to share voting and dispositive power over the shares held by Brookside Capital Partners Fund LP, and each disclaims beneficial ownership of the shares held by Brookside Capital Partners Fund LP, except to the extent of his respective proportionate pecuniary interest therein. The address of Brookside Capital Partners Fund LP is 111 Huntington Ave, Boston, MA 02199. The number of shares beneficially owned after the offering and the percentage of shares beneficially owned after the offering also include 1,000,000 shares that Brookside Capital Partners Fund LP or its affiliated entities have agreed to purchase in the offering.
- (7) Consists of (a) 160,000 shares of common stock issuable upon conversion of shares of Series B preferred stock, (b) 678,151 shares of common stock issuable upon conversion of shares of Series C preferred stock and (c) 7,065 shares of common stock issuable upon conversion of shares of Series C preferred stock issuable upon exercise of a preferred stock warrant that is exercisable as of December 31, 2013 or will become exercisable within 60 days of such date. All of the shares of preferred stock and the preferred stock warrant are held of record by S.R. One, Limited. S.R. One, Limited is a wholly-owned subsidiary of GlaxoSmithKline plc. The address of S.R. One, Limited is 161 Washington Street, Suite 500, Conshohocken, PA 19428-2077.
- (8) Consists of (a) 1,955 shares of common stock held by Oxford Bioscience Partners V, L.P. (Oxford Bioscience), (b) 287,518 shares of common stock issuable upon conversion of shares of Series A preferred stock held by Oxford Bioscience, (c) 165,253 shares of common stock issuable upon conversion of shares of Series B preferred stock held by Oxford Bioscience, (d) 279,417 shares of common stock issuable upon conversion of shares of Series C preferred stock held by Oxford Bioscience, (e) 696 shares of common stock issuable upon exercise of a common stock warrant held by Oxford Bioscience that is exercisable as of December 31, 2013 or will become exercisable within 60 days of such date, (f) 19,995 shares of common stock issuable upon conversion of shares of Series C preferred stock issuable upon exercise of a preferred stock warrant held by Oxford Bioscience that is exercisable as of December 31, 2013 or will become exercisable within 60 days of such date, (g) 43 shares of common stock held by mRNA Fund V L.P. (mRNA), (h) 6,478 shares of common stock issuable upon conversion of shares of Series A preferred stock held by mRNA, (i) 3,723 shares of common stock issuable upon conversion of shares of Series B preferred stock held by mRNA, (j) 6,295 shares of common stock issuable upon conversion of shares of Series C preferred stock held by mRNA, (k) 15

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shares of common stock issuable upon exercise of a common stock warrant held by mRNA that is exercisable as of December 31, 2013 or will become exercisable within 60 days of such date and (1) 450 shares of common stock issuable upon conversion of shares of Series C preferred stock issuable upon exercise of a preferred stock warrant held by mRNA that is exercisable as of December 31, 2013 or will become exercisable within 60 days of

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such date. Jonathan Fleming is the general partner of OBP Management V L.P., which is the general partner of both Oxford Bioscience and mRNA and may be deemed to beneficially own the shares held by Oxford Bioscience and mRNA. Each of Mr. Fleming and OBP Management V L.P. disclaims beneficial ownership of such shares, except to the extent of their respective pecuniary interests therein. The address of Oxford Bioscience and mRNA is c/o Oxford Bioscience Partners, 535 Boylston Street, Suite 402, Boston, MA 02116.

- (9) Consists of (a) 12,300 shares of common stock and (b) 105,625 shares of common stock issuable upon exercise of stock options that are exercisable as of December 31, 2013 or will become exercisable within 60 days of such date.
- (10) Dr. Halak is a managing member of One Palmer Square Associates VII, L.L.C., the general partner of Domain Partners and DP Associates, and may be deemed to share voting and dispositive power over the shares held by Domain Partners and DP Associates. Dr. Halak disclaims beneficial ownership of such shares, except to the extent of his pecuniary interest therein. The address of Dr. Halak is c/o Domain Associates, One Palmer Square, Suite 515, Princeton, NJ 08542.
- (11) Dr. Hoffman is a member of Skyline Venture Management V, LLC, the general partner of Skyline Venture Partners V, L.P., and may be deemed to share voting and dispositive power with respect to all shares of common stock held by Skyline Venture Partners V, L.P. Dr. Hoffman disclaims beneficial ownership of such shares, except to the extent of his pecuniary interest therein. The address of Dr. Hoffman is c/o Skyline Ventures, 525 University Avenue, Suite 610, Palo Alto, CA 94301.
- (12) Dr. Kolchinsky is the manager of RA Capital Management, LLC, the sole general partner of RA Capital Healthcare Fund, LP, and may be deemed to beneficially own the shares held by RA Capital Healthcare Fund, LP. Dr. Kolchinsky disclaims beneficial ownership of such shares, except to the extent of his pecuniary interest therein. The address of Dr. Kolchinsky is c/o RA Capital Management, LLC, 20 Park Plaza, Suite 1200, Boston, MA 02116.
- (13) Consists of (a) 11,651 shares of common stock issuable upon exercise of stock options held by Dennis H. Langer, M.D., J.D. that are exercisable as of December 31, 2013 or will become exercisable within 60 days of such date and (b) 180 shares of common stock, 15,000 shares of common stock issuable upon conversion of Series A preferred stock, 8,586 shares of common stock issuable upon conversion of Series B preferred stock, 71,428 shares of common stock issuable upon conversion of Series C preferred stock and 360 shares of common stock issuable upon exercise of stock options that are exercisable as of December 31, 2013 or will become exercisable within 60 days of such date owned by Langer Family Holdings, LLLP. Dennis H. Langer, M.D., J.D. is a manager of Langer Family Investments, LLC, which is the general partner of Langer Family Holdings, LLLP. Dr. Langer disclaims beneficial ownership of the shares and options owned by Langer Family Holdings, LLLP.
- (14) Consists of 26,955 shares of common stock issuable upon exercise of stock options that are exercisable as of December 31, 2013 or will become exercisable within 60 days of such date.
- (15) Dr. Miles is an executive partner of Abingworth Management Inc, a wholly-owned subsidiary of Abingworth LLP. Dr. Miles disclaims beneficial ownership of the shares owned by Abingworth Bioventures V, LP, except to the extent of his pecuniary interest therein. The address of Dr. Miles is c/o Abingworth, 890 Winter Street, Suite 150, Waltham, MA 02451.
- (16) Consists of 25,075 shares of common stock issuable upon exercise of stock options that are exercisable as of December 31, 2013 or will become exercisable within 60 days of such date.
- (17) Consists of (a) 833 shares of common stock and (b) 15,133 shares of common stock issuable upon exercise of stock options that are exercisable as of December 31, 2013 or will become exercisable within 60 days of such date.
- (18) Consists of (a) 197,572 shares of common stock held by our directors and four executive officers and issuable upon exercise of their stock options that are exercisable as of December 31, 2013 or will become exercisable within 60 days of such date and (b) 5,966,263 shares of common stock outstanding and issuable upon conversion or exercise of preferred stock, warrants and stock options that are convertible or exercisable as of December 31, 2013 or will become convertible or exercisable within 60 days of such date held by entities affiliated with certain of our directors. The number of shares beneficially owned after the offering and the percentage of shares owned after the offering also include 1,300,000 shares that entities affiliated with certain of our

directors have agreed to purchase in the offering as described in the notes above.

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DESCRIPTION OF CAPITAL STOCK

Upon the closing of this offering, our authorized capital stock will consist of 150,000,000 shares of common stock, par value \$0.0001 per share, and 5,000,000 shares of preferred stock, par value \$0.0001 per share.

As of December 31, 2013, we had outstanding 10,627,660 shares of our common stock held of record by 35 stockholders, assuming the conversion of 10,589,434 shares of preferred stock outstanding as of December 31, 2013 into shares of our common stock. Based on the number of shares of common stock outstanding as of December 31, 2013, and assuming the conversion of all outstanding shares of our preferred stock, there will be 16,627,660 shares of common stock outstanding upon the closing of this offering (17,527,660 if the underwriters exercise in full their option to purchase additional shares of common stock).

As of December 31, 2013, there were 1,621,678 shares of common stock subject to outstanding stock options, 2,198 shares of common stock subject to outstanding warrants to purchase common stock and 133,103 shares of preferred stock subject to outstanding warrants to purchase preferred stock.

The following description of our capital stock is intended as a summary only and is qualified in its entirety by reference to our amended and restated certificate of incorporation and amended and restated bylaws, which will become effective upon the closing of this offering, and to the applicable provisions of the Delaware General Corporation Law, as amended. Copies of our amended and restated certificate of incorporation and amended and restated bylaws are filed as exhibits to the registration statement, of which this prospectus forms a part. We refer in this section to our amended and restated certificate of incorporation as our certificate of incorporation, and we refer to our amended and restated bylaws as our bylaws.

Common Stock

Voting rights

Holders of our common stock are entitled to one vote for each share of common stock held of record for the election of directors and on all matters submitted to a vote of stockholders. In the election of directors, a plurality of the votes cast at a meeting of stockholders is sufficient to elect a director. Our stockholders do not have cumulative voting rights in the election of directors. Accordingly, holders of a majority of the voting shares are able to elect all of the directors. In all other matters, except as noted below under **Anti-takeover effects of Delaware law**, our certificate of incorporation and our bylaws, a majority vote of common stockholders is generally required to take action under our certificate of incorporation and bylaws.

Dividends

Holders of our common stock are entitled to receive dividends ratably, if any, as may be declared by our board of directors out of legally available funds, subject to any preferential dividend rights of any preferred stock then outstanding.

Liquidation

Upon our dissolution, liquidation or winding up, holders of our common stock are entitled to share ratably in our net assets legally available after the payment of all our debts and other liabilities, subject to the preferential rights of any preferred stock then outstanding.

Other rights and preferences

Holders of our common stock have no preemptive, subscription or conversion rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

As of December 31, 2013, there were 855,996 shares of our Series A preferred stock, 1,162,021 shares of our Series B preferred stock and 8,571,417 shares of our Series C preferred stock outstanding. Upon the closing of this offering, all outstanding shares of our preferred stock will be converted into shares of our common stock on a one-for-one basis.

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Upon the closing of this offering, our board of directors will be authorized, without action by the stockholders, to designate and issue up to an aggregate of 5,000,000 shares of preferred stock in one or more series. The board of directors can fix the rights, preferences and privileges of the shares of each series and any of its qualifications, limitations or restrictions. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of common stock. The issuance of preferred stock, while providing flexibility in connection with possible future financings and acquisitions and other corporate purposes could, under certain circumstances, have the effect of delaying or preventing a change in control of our company and might harm the market price of our common stock. Upon the closing of this offering, no shares of preferred stock will be outstanding, and we have no present plan to issue any shares of preferred stock.

Warrants

As of December 31, 2013, we had five warrants to purchase an aggregate of 2,198 shares of our common stock with an exercise price of \$250 per share. Each of these warrants is exercisable at any time on or before June 17, 2020.

As of December 31, 2013, we had a warrant to purchase 21,000 shares of our Series A preferred stock with an exercise price of \$25 per share. This warrant is exercisable at any time on or before the earlier of March 25, 2019 or the third anniversary of the closing of this offering. Upon the closing of this offering, this warrant will become exercisable for 21,000 shares of our common stock.

As of December 31, 2013, we had a warrant to purchase 26,400 shares of our Series B preferred stock with an exercise price of \$25 per share. This warrant is exercisable at any time on or before the earlier of July 6, 2021 or the third anniversary of the closing of this offering. Upon the closing of this offering, this warrant will become exercisable for 26,400 shares of our common stock.

As of December 31, 2013, we had seven warrants to purchase an aggregate of 85,703 shares of our Series C preferred stock with an exercise price of \$7 per share. Each of these warrants is exercisable at any time on or before June 26, 2018. Upon the closing of this offering, these warrants will become exercisable for 85,703 shares of our common stock.

Registration Rights

We are party to an amended and restated registration rights agreement dated as of July 30, 2013, pursuant to which certain of our stockholders are entitled to demand, Form S-3 and piggyback registration rights. Such stockholders have agreed not to exercise their registration rights during the lock-up period for this offering. See [Shares Eligible for Future Sale](#) [Lock-up agreements](#).

Demand registration rights

At any time after the earlier of December 31, 2018 and 180 days after the closing of this offering, the holders of at least a majority of the registrable securities have the right to demand us to file, for no more than two times, a registration statement on Form S-1 to register all or a portion of their registrable securities.

Form S-3 registration rights

After the closing of this offering, the holders of at least 25 percent of the registrable securities have the right to demand us to file an unlimited number of registration statements on Form S-3 provided that the anticipated aggregate offering price of the registrable securities to be sold under the registration statement on Form S-3 exceeds \$3.0 million, net of underwriting discounts and commissions.

Piggyback registration rights

If we propose to register any of our securities under the Securities Act of 1933, as amended, for sale to the public other than certain exceptions, the holders of registrable securities are entitled to receive notice of such registration and to request that we include their registrable securities for resale in the registration statement. The underwriters of the offering will have the right to limit the number of shares to be included in such registration.

Expenses of registration; indemnification

We are generally required to bear all registration expenses incurred in connection with the demand, Form S-3 and piggyback registrations described above, other than underwriting commissions and discounts. The amended and restated registration rights agreement contain customary

indemnification provisions with respect to registration rights.

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Termination of registration rights

The demand, Form S-3 and piggyback registration rights described above will terminate five years after the closing of this offering. In addition, the registration rights of a holder of registrable securities will expire if all of the holder's registrable securities may be sold in a three-month period under Rule 144 of the Securities Act of 1933, as amended.

Anti-Takeover Effects of Delaware Law, Our Certificate of Incorporation and Our Bylaws

Our certificate of incorporation and bylaws include a number of provisions that may have the effect of encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Removal of directors

Our certificate of incorporation and bylaws provide that subject to any limitations imposed by law and the rights of the holders of any series of our preferred stock, the board of directors or any individual director may be removed from office at any time without cause by the affirmative vote of the holders of a majority of the voting power of all the then-outstanding shares of voting stock of the Company, entitled to vote at an election of directors.

No written consent of stockholders

Our bylaws provide that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting.

Meetings of stockholders

Our bylaws provide that special meetings of stockholders, which the Company is not obligated to call more than once per calendar year, may only be called 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). In addition, our bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance notice requirements

Our bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than the close of business on the ninetieth (90th) day nor earlier than the close of business on the one hundred twentieth (120th) day prior to the first anniversary of the annual meeting for the preceding year. The notice must contain certain information specified in the bylaws. These provisions may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed. These provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.

Amendment to certificate of incorporation and bylaws

Our certificate of incorporation provide that the affirmative votes of the holders of at least a majority of the voting power of all of the the-outstanding shares of our voting stock will be required to amend certain provisions of our certificate of incorporation, including provisions relating to the size of our board of directors, removal of directors, special meeting of stockholders and actions by written consent. The affirmative votes of the holders of at least a majority of the voting power of all of the then-outstanding shares of our voting stock will be required to amend or repeal our bylaws. In addition, our bylaws may be amended by our board of directors, subject to any limitations set forth in the bylaws.

Blank check preferred stock

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Our certificate of incorporation provides for 5,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might

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dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Section 203 of the Delaware General Corporation Law

Upon the closing of this offering, we will be subject to the provisions of Section 203 of the Delaware General Corporation Law, as amended. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A business combination includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15 percent or more of the corporation's voting stock.

Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- n before the stockholder became interested, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- n upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85 percent of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or
- n at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least 66 2/3 percent of the outstanding voting stock which is not owned by the interested stockholder.

A Delaware corporation may opt out of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or bylaws resulting from a stockholders' amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

Delaware as sole and exclusive forum

Our bylaws provide, that unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware shall, to the fullest extent permitted by law, be the sole and exclusive forum for (i) any derivative action or proceeding brought on behalf of us, (ii) any action asserting a claim of breach of a fiduciary duty owed by, or otherwise wrongdoing by, any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, as amended, or our certificate of incorporation or bylaws, (iv) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws, or (v) any action asserting a claim against us or any of our directors, officers or employees governed by the internal affairs doctrine.

The NASDAQ Global Select Market Listing

Our common stock has been approved for listing on The NASDAQ Global Select Market under the trading symbol DRNA.

Transfer Agent and Registrar

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The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent and registrar's address is 6201 15th Avenue, Brooklyn, NY 11219.

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SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock, and we cannot assure you that a liquid trading market for our common stock will develop or be sustained after this offering. Future sales of substantial numbers of shares of our common stock, including shares issued upon exercise of outstanding options or warrants, in the public market after this offering, or the perception that those sales may occur, could cause the prevailing market price for our common stock to fall or impair our ability to raise equity capital at a time and price we deem appropriate. As described below, substantially all of our shareholders will not be subject to lock-up agreements in connection with this offering. As a result, the only limitations on the salability of these shares will be due to restrictions imposed by Rules 144 or 701 under the Securities Act and a significant number of shares of our common stock will be available for sale in the public market immediately after the completion of this offering.

Sale of Restricted Shares

As of December 31, 2013, based on the number of shares of our common stock then outstanding, upon the closing of this offering and assuming (1) the conversion of our outstanding preferred stock into common stock, (2) no exercise of the underwriters' option to purchase additional shares of common stock, and (3) no exercise of outstanding options or warrants, we would have had outstanding an aggregate of approximately 16,627,660 shares of common stock. Of these shares, all of the 6,000,000 shares of common stock to be sold in this offering, and any shares sold upon exercise of the underwriters' option to purchase additional shares will be freely tradable in the public market without restriction or further registration under the Securities Act unless the shares are held by any of our affiliates as such term is defined in Rule 144 of the Securities Act. All remaining shares of common stock held by existing stockholders immediately prior to the completion of this offering will be restricted securities as such term is defined in Rule 144. These restricted securities were issued and sold by us, or will be issued and sold by us, in private transactions and are eligible for public sale only if registered under the Securities Act or if they qualify for an exemption from registration under the Securities Act, including the exemptions provided by Rule 144 or Rule 701, which rules are summarized below.

As a result of the lock-up agreements referred to below and the provisions of Rule 144 and Rule 701 under the Securities Act, based on 10,627,660 shares of our common stock outstanding as of December 31, 2013 assuming the conversion of our preferred stock, the shares of our common stock (excluding the shares sold in this offering) that will be available for sale in the public market are as follows:

- n beginning on the date of this prospectus, approximately 701,085 shares of our common stock, or 6.6 percent of such total outstanding shares of our common stock as of December 31, 2013, will be immediately available for sale in the public market;
- n beginning 90 days after the date of this prospectus, an additional approximately 9,913,442 shares of our common stock, or 93.3 percent of such total outstanding shares of our common stock as of December 31, 2013, will be eligible for sale in the public market from time to time thereafter, subject in some cases to the volume and other restrictions of Rule 144 as described below; and
- n beginning 180 days after the date of this prospectus, the remainder of the shares of our common stock will be eligible for sale in the public market due to the expiration of the lock-up agreements between our executive officers and the underwriters, provided that the representatives of the underwriters may waive the provisions of these lock-up agreements and allow these stockholders to sell their shares earlier.

Rule 144

In general, under Rule 144 under the Securities Act, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person (or persons whose shares are aggregated) who is not deemed to have been an affiliate of ours at any time during the three months preceding a sale, and who has beneficially owned restricted securities within the meaning of Rule 144 for at least six months (including any period of consecutive ownership of preceding non-affiliated holders) would be entitled to sell those shares, subject only to the availability of current public information about us. A non-affiliated person who has beneficially owned restricted securities within the meaning of Rule 144 for at least one year would be entitled to sell those shares without regard to the provisions of Rule 144.

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A person (or persons whose shares are aggregated) who is deemed to be an affiliate of ours and who has beneficially owned restricted securities within the meaning of Rule 144 for at least six months would be entitled to sell within any three-month period a number of shares that does not exceed the greater of one percent of the then outstanding shares of our common stock or the average weekly trading volume of our common stock reported through The NASDAQ Global Select Market during the four calendar weeks preceding such sale. Such sales are also subject to certain manner of sale provisions, notice requirements and the availability of current public information about us.

Rule 701

In general and subject to the terms of the lock-up agreements, under Rule 701 of the Securities Act, most of our employees, consultants or advisors who purchased shares from us in connection with a qualified compensatory stock plan or other written agreement are eligible to resell those shares 90 days after the date of this prospectus in reliance on Rule 144, but without compliance with the holding period or certain other restrictions contained in Rule 144.

Lock-Up Agreements

We and our executive officers have agreed, subject to specified exceptions, not to, directly or indirectly, sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open put equivalent position within the meaning of Rule 16a-1(h) under the Securities Exchange Act of 1934, as amended, or otherwise dispose of any shares of common stock, options or warrants to acquire shares of common stock, or securities exchangeable or exercisable for or convertible into shares of common stock currently or hereafter owned either of record or beneficially, or publicly announce an intention to do any of the foregoing for a period of 180 days after the date of this prospectus without the prior written consent of Jefferies LLC and Leerink Partners LLC. This restriction terminates after the close of trading of the common stock on and including the 180th day after the date of this prospectus. Jefferies LLC and Leerink Partners LLC may, in their sole discretion and at any time or from time to time before the termination of the 180-day period release all or any portion of the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any person who will execute a lock-up agreement in connection with this offering, providing consent to the sale of shares prior to the expiration of the lock-up period. We have entered into a similar agreement with the representatives of the underwriters, except that we may be permitted to issue shares of our common stock for certain strategic purposes.

Substantially all of our shareholders, warrant holders and option holders will not be subject to any lock-up agreements.

Equity Incentive Plans

We intend to file with the SEC a registration statement under the Securities Act covering the shares of common stock that we may issue upon exercise of outstanding options reserved for issuance under our 2007 Plan and our 2010 Plan. Such registration statement is expected to be filed and become effective as soon as practicable after the completion of this offering. Accordingly, shares registered under such registration statement will be available for sale in the open market following its effective date, subject to Rule 144 volume limitations and the lock-up agreements described above, if applicable.

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MATERIAL U.S. FEDERAL TAX CONSEQUENCES FOR NON-U.S. HOLDERS OF COMMON STOCK

The following is a summary of the material U.S. federal income and estate tax consequences relating to the ownership and disposition of our common stock by non-U.S. holders (as defined below) who purchase our common stock in this offering and hold such common stock as capital assets (generally for investment). This discussion is based on currently existing provisions of the Internal Revenue Code of 1986, as amended, applicable U.S. Treasury regulations promulgated thereunder, judicial decisions and rulings and pronouncements of the U.S. Internal Revenue Service, or the IRS, all as in effect on the date hereof and all of which are subject to change, possibly with retroactive effect, or subject to different interpretation. This discussion does not address all the tax consequences that may be relevant to specific holders in light of their particular circumstances or to holders subject to special treatment under U.S. federal income or estate tax laws (such as financial institutions, insurance companies, tax-exempt organizations, controlled foreign corporations, passive foreign investment companies, retirement plans, partnerships or entities treated as such for U.S. federal income tax purposes and their partners, dealers in securities, brokers, certain former U.S. citizens or long-term residents or persons who have acquired our common stock as part of a straddle, hedge, conversion transaction or other integrated investment). This discussion does not address the state, local or foreign tax or U.S. federal non-income or estate tax consequences relating to the ownership and disposition of our common stock. You are urged to consult your own tax advisor regarding the U.S. federal tax consequences of owning and disposing of our common stock, as well as the applicability and effect of any state, local or foreign tax laws.

As used in this discussion, the term **non-U.S. holder** refers to a beneficial owner of our common stock that for U.S. federal income tax purposes is not:

- n an individual who is a citizen or resident of the U.S.;
- n corporation (or other entity taxable as a corporation) created or organized in or under the laws of the U.S., any state thereof, or the District of Columbia or otherwise treated as such for U.S. federal income tax purposes;
- n an estate the income of which is subject to U.S. federal income tax regardless of the source thereof; or
- n a trust (a) with respect to which a court within the U.S. is able to exercise primary supervision over its administration and one or more U.S. persons have the authority to control all its substantial decisions or (b) that has in effect a valid election under applicable U.S. Treasury regulations to be treated as a U.S. person.

An individual may be treated as a resident of the U.S., among other ways, if present in the U.S. on at least 31 days in a calendar year and for an aggregate of at least 183 days during the three-year period ending in that calendar year (counting for such purposes all the days present in the current year, one-third of the days present in the immediately preceding year and one-sixth of the days present in the second preceding year).

If a partnership or other entity or arrangement treated as a partnership for U.S. federal income tax purposes holds our common stock, the tax treatment of a partner will generally depend upon the status of the partner and the activities of the partnership. If you are a partner of a partnership holding our common stock, we urge you to consult your own tax advisor.

Dividends

We do not anticipate paying dividends on our common stock in the foreseeable future. See the section titled **Dividend Policy** elsewhere in this prospectus. If we make a distribution of cash or property, those payments will constitute dividends for U.S. tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed both our current and our accumulated earnings and profits, they will constitute a return of capital and will first reduce a non-U.S. holder's basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock.

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Dividends paid by us to a non-U.S. holder, to the extent treated as dividends for U.S. federal income tax purposes, generally will be subject to U.S. federal withholding tax at a 30 percent rate, unless (i) an applicable income tax treaty reduces or eliminates such tax, and a non-U.S. holder provides us with an IRS Form W-8BEN (or successor form) properly certifying its entitlement to the benefit of such treaty or (ii) the dividends are effectively connected with a non-U.S. holder's conduct of a trade or business in the U.S. and, where a tax treaty so provides, the dividends are attributable to a U.S. permanent establishment of such non-U.S. holder, and the non-U.S. holder provides us with an IRS Form W-8ECI (or successor form). In the latter case, a non-U.S. holder generally will be subject to U.S. federal income tax with respect to such dividends in the same manner as a U.S. person, unless otherwise provided in an applicable income tax treaty. Additionally, a non-U.S. holder that is a corporation may be subject to a branch profits tax on its after-tax effectively connected dividend income at a rate of 30 percent (or at a reduced rate under an applicable income tax treaty). If a non-U.S. holder is eligible for a reduced rate of U.S. federal withholding tax pursuant to an income tax treaty, such non-U.S. holder may obtain a refund of any excess amount withheld by timely filing an appropriate claim for refund with the IRS.

Sale, Exchange or Other Disposition

Generally, a non-U.S. holder will not be subject to U.S. federal income tax on gain realized upon the sale, exchange or other disposition of our common stock unless (i) such non-U.S. holder is an individual present in the U.S. for 183 days or more in the taxable year of the sale, exchange or other disposition and certain other conditions are met, (ii) the gain is effectively connected with such non-U.S. holder's conduct of a trade or business in the U.S. and, where a tax treaty so provides, the gain is attributable to a U.S. permanent establishment of such non-U.S. holder or (iii) we are or have been a U.S. real property holding corporation for U.S. federal income tax purposes at any time during the shorter of the five-year period ending on the date of disposition or the period that the non-U.S. holder held our common stock and either (a) our common stock has ceased to be traded on an established securities market prior to the beginning of the calendar year in which the sale, exchange or other disposition occurs or (b) the non-U.S. holder owns (actually or constructively) more than five percent of our common stock. We believe that we are not a U.S. real property holding corporation, and we do not anticipate becoming a U.S. real property holding corporation.

A non-U.S. holder described in (i) above will be required to pay a flat 30 percent tax (or such lower rate as may be specified by an applicable income tax treaty) on the gain derived from the sale, which tax may be offset by U.S. source capital losses. A non-U.S. holder described in (ii) above will be required to pay tax on the net gain derived from the sale under regular graduated U.S. federal income tax rates, and corporate non-U.S. holders described in (ii) may be subject to the branch profits tax at a 30 percent rate or such lower rate as may be specified by an applicable income tax treaty. Non-U.S. holders should consult any applicable income tax or other treaties that may provide for different rules.

Federal Estate Tax

Common stock owned or treated as owned by an individual who is a non-U.S. holder at the time of his or her death generally will be included in the individual's gross estate for U.S. federal estate tax purposes and may be subject to U.S. federal estate tax unless an applicable estate tax treaty provides otherwise.

Information Reporting and Backup Withholding

Information reporting and backup withholding (at the then applicable rate) may apply to certain payments made to a non-U.S. holder on or with respect to our common stock, unless the non-U.S. holder certifies as to its status as a non-U.S. holder under penalties of perjury or otherwise establishes an exemption and certain other conditions are satisfied. Pursuant to applicable income tax treaties or other agreements, the IRS may also make these information reports available to tax authorities in the non-U.S. holder's country of residence. Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder will generally be allowed as a refund or a credit against such non-U.S. holder's U.S. federal income tax liability, provided that the required information is timely furnished to the IRS and other applicable requirements are satisfied.

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FATCA Withholding

The Foreign Account Tax Compliance Act (FATCA) will impose a U.S. federal withholding tax of 30 percent on certain payments to foreign financial institutions, investment funds and other non-U.S. persons that fail to comply with certain information reporting and certification requirements pertaining to their direct and indirect U.S. securityholders and/or U.S. accountholders. Such payments would include our dividends and the gross proceeds from the sale or other disposition of our common stock. Under recently issued final Treasury Regulations, this withholding will apply to payments of dividends on our common stock made on or after July 1, 2014 and to payments of gross proceeds from a sale or other disposition of our common stock made on or after January 1, 2017. Prospective investors are encouraged to consult with their own tax advisors regarding the possible implications of this legislation on their investment in our common stock.

The preceding discussion of U.S. federal income tax considerations is for general information only. It is not tax advice. Each prospective investor should consult its own tax advisor regarding the particular U.S. federal, state and local and foreign tax consequences of acquiring, holding and disposing of our common stock, including the consequences of any proposed change in applicable law.

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Subject to the terms and conditions set forth in the underwriting agreement, dated January 29, 2014, among us and Jefferies LLC and Leerink Partners LLC, as the representatives of the underwriters named below and, together with Stifel, Nicolaus & Company, Incorporated, the joint book-running managers of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of shares of common stock shown opposite its name below:

UNDERWRITERS	NUMBER OF SHARES
Jefferies LLC	2,250,000
Leerink Partners LLC	2,250,000
Stifel, Nicolaus & Company, Incorporated	900,000
Robert W. Baird & Co. Incorporated	600,000
Total	6,000,000

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares of common stock if any of them are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in the common stock as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the common stock, that you will be able to sell any of the common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the shares of common stock subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part. In addition, the underwriters have advised us that they do not intend to confirm sales to any account over which they exercise discretionary authority.

Commission and Expenses

The underwriters have advised us that they propose to offer the shares of common stock to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers, which may include the underwriters, at that price less a concession not in excess of \$0.63 per share of common stock. After the offering, the initial public offering price and concession to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus.

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The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	PER SHARE		TOTAL	
	WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES	WITH OPTION TO PURCHASE ADDITIONAL SHARES	WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES	WITH OPTION TO PURCHASE ADDITIONAL SHARES
Public offering price	\$ 15.00	\$ 15.00	\$ 90,000,000	\$ 103,500,000
Underwriting discounts and commissions paid by us	\$ 1.05	\$ 1.05	\$ 6,300,000	\$ 7,245,000
Proceeds to us, before expenses	\$ 13.95	\$ 13.95	\$ 83,700,000	\$ 96,255,000

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$3.4 million, including the reimbursement of certain underwriters' expenses and the payment to another investment banking firm as described below.

We have agreed to reimburse the underwriters for certain of their expenses in an amount of up to \$40,000 as set forth in the underwriting agreement.

Prior to our engagement of the underwriters, we engaged Healthios Capital Markets, LLC, an investment banking firm, for an offering of our securities subject to certain conditions and limitations. We terminated our arrangement with that investment banking firm in July 2013. In relation to this offering, we have agreed to pay this investment banking firm a fee of \$350,000 in satisfaction of the compensatory terms of that arrangement. This investment banking firm had previously provided financial advisory services to us, but will not be participating in the underwriting or selling of securities in this offering. We have agreed to indemnify the underwriters in this offering against any liabilities arising from any claims related to that arrangement.

Determination of Offering Price

Prior to this offering, there has not been a public market for our common stock. Consequently, the initial public offering price for our common stock will be determined by negotiations between us and the representatives. Among the factors to be considered in these negotiations will be prevailing market conditions, our financial information, market valuations of other companies that we and the underwriters believe to be comparable to us, estimates of our business potential, the present state of our development and other factors deemed relevant.

We offer no assurances that the initial public offering price will correspond to the price at which the common stock will trade in the public market subsequent to the offering or that an active trading market for the common stock will develop and continue after the offering.

Listing

Our common stock has been approved for listing on The NASDAQ Global Select Market under the trading symbol DRNA.

Stamp Taxes

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If you purchase shares of common stock offered in this prospectus, you may be required to pay stamp taxes and other charges under the laws and practices of the country of purchase, in addition to the offering price listed on the cover page of this prospectus.

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase, from time to time, in whole or in part, up to an aggregate of 900,000 shares from us at the public offering price set forth on the cover page of this prospectus, less underwriting discounts and commissions. If the underwriters exercise

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this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares proportionate to that underwriter's initial purchase commitment as indicated in the table above. This option may be exercised only if the underwriters sell more shares than the total number set forth on the cover page of this prospectus.

No Sales of Similar Securities

We and our executive officers have agreed, subject to specified exceptions, not to directly or indirectly:

- n sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open put equivalent position within the meaning of Rule 16a-1(h) under the Securities Exchange Act of 1934, as amended, or
- n otherwise dispose of any shares of common stock, options or warrants to acquire shares of common stock, or securities exchangeable or exercisable for or convertible into shares of common stock currently or hereafter owned either of record or beneficially, or
- n publicly announce an intention to do any of the foregoing for a period of 180 days after the date of this prospectus without the prior written consent of Jefferies LLC and Leerink Partners LLC.

This restriction terminates after the close of trading of the common stock on and including the 180th day after the date of this prospectus.

Jefferies LLC and Leerink Partners LLC may, in their sole discretion and at any time or from time to time before the termination of the 180-day period, release all or any portion of the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any person who will execute a lock-up agreement in connection with this offering, providing consent to the sale of shares prior to the expiration of the lock-up period.

Substantially all of our shareholders, warrant holders and option holders will not be subject to any lock-up agreements. See [Shares Eligible For Future Sale](#) and [Risk Factors](#). Substantially all of our outstanding shares will not be subject to lock-up agreements in connection with this offering. The sale of a significant number of our shares may cause the market price of our common stock to drop significantly.

Stabilization

The underwriters have advised us that, pursuant to Regulation M under the Securities Exchange Act of 1934, as amended, certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either covered short sales or naked short sales.

Covered short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

Naked short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of shares of common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriter's purchases to cover the

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syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our common stock on The NASDAQ Global Select Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Distribution

A prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares of common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' web sites and any information contained in any other web site maintained by any of the underwriters is not part of this prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Directed Share Program

At our request, the underwriters have reserved for sale at the initial public offering price up to 150,000 shares of common stock sold in this offering for employees, directors and other persons associated with us who have expressed an interest in purchasing shares in the offering. The number of shares of common stock available for sale to the general public in the offering will be reduced to the extent these persons purchase the directed shares in the program. Any directed shares not so purchased will be offered by the underwriters to the general public on the same terms as the other shares. These shares will not be subject to any lock-up arrangement with any underwriters, except to the extent purchased by one or more of our executive officers, who have entered into lock-up agreements described above. For any such participants who have entered into lock-up agreements described above, the lock-up agreements contemplated therein shall govern with respect to their purchases of shares of common stock in the program. The representatives in their sole discretion may release any of the securities subject to these lock-up agreements at any time. We have agreed to indemnify the underwriters against certain liabilities and expenses, including liabilities under the Securities Act, in connection with sales of the directed shares.

Other Activities and Relationships

The underwriters and certain of their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their respective affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and certain of their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their

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customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common stock offered hereby. Any such short positions could adversely affect future trading prices of the common stock offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Disclaimers About Non-U.S. Jurisdictions

European Economic Area

In relation to each member state of the European Economic Area which has implemented the Prospectus Directive (Relevant Member State), an offer to the public of any common shares which are the subject of the offering contemplated by this prospectus may not be made in that Relevant Member State except that an offer to the public in that Relevant Member State of any common shares may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

- (a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- (b) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the underwriters or the underwriters nominated by us for any such offer; or
- (c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of common shares shall require us or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this provision, the expression an offer common shares to the public in relation to the common shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the common shares to be offered so as to enable an investor to decide to purchase or subscribe to the common shares, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (Order) and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated (each such person being referred to as a relevant person).

This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

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LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed on for us by our counsel, O Melveny & Myers LLP, Menlo Park, California. Certain legal matters in connection with this offering will be passed upon for the underwriters by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts.

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EXPERTS

The financial statements as of December 31, 2011 and 2012, and for each of the two years in the period ended December 31, 2012, included in this prospectus, have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report appearing herein. Such financial statements have been so included in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

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WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed a registration statement on Form S-1 with the Securities and Exchange Commission with respect to the registration of the common stock offered for sale by this prospectus. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information about us, the common stock we are offering by this prospectus and related matters, you should review the registration statement, including the exhibits filed as a part of the registration statement. Statements contained in this prospectus about the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and in each instance we refer you to the full text of such contract or other document filed as an exhibit to the registration statement. A copy of the registration statement and the exhibits that were filed with the registration statement may be inspected without charge at the public reference facilities maintained by the Securities and Exchange Commission at 100 F Street N.E., Washington, D.C. 20549, and copies of all or any part of the registration statement may be obtained from the Securities and Exchange Commission upon payment of the prescribed fee. Information on the operation of the public reference facilities may be obtained by calling the Securities and Exchange Commission at 1-800-SEC-0330. The Securities and Exchange Commission maintains a website that contains reports, proxy and information statements and other information regarding registrants that file electronically with the Securities and Exchange Commission. The address of the site is <http://www.sec.gov>. You may also request copies of these filings, at no cost, by telephone at (617) 621-8097 or by mail to: Dicerna Pharmaceuticals, Inc., 480 Arsenal Street, Building 1, Suite 120, Watertown, Massachusetts 02472, Attention: Chief Financial Officer.

We will become subject to the information and periodic reporting requirements of the Exchange Act, and, in accordance with such requirements, file periodic reports and other information with the Securities and Exchange Commission. These periodic reports and other information are available for inspection and copying at the regional offices, public reference facilities and website of the Securities and Exchange Commission referred to above. We intend to furnish our stockholders with annual reports containing financial statements audited by our independent registered accounting firm. We also maintain a website at <http://www.dicerna.com>, at which you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the Securities and Exchange Commission. The information contained in, or that can be accessed through, our website is not part of this prospectus.

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DICERNA PHARMACEUTICALS, INC.

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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 balance sheets of Dicerna Pharmaceuticals, Inc. (the Company) as of December 31, 2012 and 2011, and the related statements of operations, redeemable convertible preferred stock and stockholders' deficit, and cash flows for the two years then ended. 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 the Company as of December 31, 2012 and 2011, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2012, in conformity with accounting principles generally accepted in the United States of America.

/s/ Deloitte & Touche LLP

Boston, Massachusetts

November 8, 2013

Table of Contents**DICERNA PHARMACEUTICALS, INC.****Balance Sheets**

As of December 31, 2011 and 2012 and September 30, 2013

(In thousands, except share data and par value)

	DECEMBER 31, 2011	DECEMBER 31, 2012	SEPTEMBER 30, 2013	PRO FORMA SEPTEMBER 30, 2013 <i>(Unaudited)</i>
ASSETS				
CURRENT ASSETS:				
Cash and cash equivalents	\$ 22,490	\$ 3,670	\$ 54,712	\$ 54,712
Research and license agreement receivable	161	5,018		
Prepaid expenses and other current assets	372	344	413	413
Total current assets	23,023	9,032	55,125	55,125
NONCURRENT ASSETS:				
Property and equipment net	1,314	883	683	683
Restricted cash	264	264	264	264
Other assets	36	12		
Total noncurrent assets	1,614	1,159	947	947
TOTAL	\$ 24,637	\$ 10,191	\$ 56,072	\$ 56,072
LIABILITIES AND STOCKHOLDERS DEFICIT				
CURRENT LIABILITIES:				
Accounts payable	\$ 1,414	\$ 1,198	\$ 1,557	\$ 1,557
Current portion of long-term debt	2,834	4,140	4,471	4,471
Deferred revenue	830			
Deferred rent		63	14	14
Accrued expenses and other current liabilities	221	270	518	518
Total current liabilities	5,299	5,671	6,560	6,560
NONCURRENT LIABILITIES:				
Long-term debt net of current portion	8,735	4,660	1,407	1,407
Preferred stock warrant liability	800	331	436	
Deferred revenue net of current portion	184			
Deferred rent net of current portion	101			
Total noncurrent liabilities	9,820	4,991	1,843	1,407
TOTAL LIABILITIES	15,119	10,662	8,403	7,967

COMMITMENTS AND CONTINGENCIES (Note 13)

REDEEMABLE CONVERTIBLE PREFERRED STOCK, \$0.0001 PAR VALUE AUTHORIZED 11,070,000 SHARES:

Series A 880,000 shares designated; 855,996 shares issued and outstanding at December 31, 2011 and 2012 and September 30, 2013 (unaudited), and no shares issued and outstanding pro forma (unaudited), (aggregate liquidation preference of	27,990	29,728	21,400
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\$29,775 at December 31, 2012, and \$21,400 at September 30, 2013 (unaudited));

no shares issued and outstanding pro forma (unaudited)

Series B 1,190,000 shares designated; 1,162,021 shares issued and outstanding at December 31, 2011 and 2012 and September 30, 2013 (unaudited), and no shares issued and outstanding pro forma (unaudited); no shares issued and outstanding pro forma (unaudited) (aggregate liquidation preference of \$34,578 at December 31, 2012 and \$29,050 at September 30, 2013 (unaudited))

32,161 34,520 29,050

Series C No shares designated, issued and outstanding at December 31, 2011 and 2012 and 9,000,000 shares designated; 8,571,417 shares issued and outstanding at September 30, 2013 (unaudited), and no shares issued and outstanding pro forma (unaudited), (aggregate liquidation preference of \$60,000 at September 30, 2013 (unaudited)); no shares issued and outstanding pro forma (unaudited)

59,787

STOCKHOLDERS DEFICIT:

Common stock, \$0.0001 par value authorized 15,000,000 shares; issued 27,697 and 27,978 shares at December 31, 2011 and 2012, respectively, and outstanding 27,522 and 27,853 shares at December 31, 2011 and 2012, respectively, issued and outstanding 28,093 shares at September 30, 2013 (unaudited)

1 1 1 2

Additional paid-in capital

16,177 126,849

Accumulated deficit

(50,634) (64,720) (78,746) (78,746)

Total stockholders deficit

(50,633) (64,719) (62,568) 48,105

TOTAL

\$ 24,637 \$ 10,191 \$ 56,072 \$ 56,072

See notes to financial statements.

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Table of Contents**DICERNA PHARMACEUTICALS, INC.****Statements of Operations**

For the years ended December 31, 2011 and 2012 and for the nine months ended September 30, 2012 and 2013

(In thousands, except share data and per share data)

	YEAR ENDED DECEMBER 31,		NINE MONTHS ENDED SEPTEMBER 30,	
	2011	2012	2012	2013
			<i>(Unaudited)</i>	
Revenue	\$ 7,908	\$ 7,015	\$ 762	\$
Operating expenses:				
Research and development	10,705	11,565	8,078	7,364
General and administrative	4,816	4,700	3,631	3,577
Total operating expenses	15,521	16,265	11,709	10,941
Loss from operations	(7,613)	(9,250)	(10,947)	(10,941)
Other income (expense):				
Preferred stock warrant remeasurement	51	469	352	219
Interest income	3	2	1	1
Loss on extinguishment of debt				(318)
Interest expense	(997)	(1,342)	(1,040)	(760)
Total other income (expense)	(943)	(871)	(687)	(858)
Net loss	\$ (8,556)	\$ (10,121)	\$ (11,634)	\$ (11,799)
Less: Accretion and dividends on redeemable convertible preferred stock	\$ 4,099	\$ 4,097	\$ 3,068	\$ 2,379
Net loss attributable to common stockholders	\$ (12,655)	\$ (14,218)	\$ (14,702)	\$ (14,178)
Net loss per share attributable to common stockholders Basic and diluted	\$ (492.76)	\$ (516.00)	\$ (533.86)	\$ (505.45)
Weighted average shares outstanding Basic and diluted	25,682	27,554	27,539	28,050
Pro forma net loss per share attributable to common stockholders (unaudited) Basic and diluted		\$ (4.95)		\$ (2.65)
Pro forma weighted average shares outstanding (unaudited) Basic and diluted		2,045,579		4,444,333

See notes to financial statements.

Table of Contents**DICERNA PHARMACEUTICALS, INC.****Statements of Redeemable Convertible Preferred Stock and Stockholders' Deficit**

For the years ended December 31, 2011 and 2012 and for the nine months ended September 30, 2013

(In thousands, except share data and par value)

	SERIES A REDEEMABLE CONVERTIBLE PREFERRED STOCK \$0.0001 PAR VALUE		SERIES B REDEEMABLE CONVERTIBLE PREFERRED STOCK \$0.0001 PAR VALUE		SERIES C REDEEMABLE CONVERTIBLE PREFERRED STOCK \$0.0001 PAR VALUE		COMMON STOCK \$0.0001 PAR VALUE		ADDITIONAL PAID-IN CAPITAL	ACCUMULATED DEFICIT	TOTAL STOCKHOLDERS' DEFICIT
	SHARES	AMOUNT	SHARES	AMOUNT	SHARES	AMOUNT	SHARES	AMOUNT			
BALANCE January 1, 2011	855,996	\$ 26,252	1,162,021	\$ 29,800		\$	25,199	\$ 1		\$ (38,222)	\$ (38,221)
Accretion of preferred stock issuance costs		26		37					(63)		(63)
Accrued dividends		1,712		2,324					(180)	(3,856)	(4,036)
Vesting of restricted common stock							73		4		4
Sale of restricted common stock							25		10		10
Stock-based compensation									169		169
Exercise of common stock options							2,225		60		60
Net loss										(8,556)	(8,556)
BALANCE December 31, 2011	855,996	27,990	1,162,021	32,161			27,522	1		(50,634)	(50,633)
Accretion of preferred stock issuance costs		26		35					(61)		(61)
Accrued dividends		1,712		2,324					(71)	(3,965)	(4,036)
Vesting of restricted common stock							50		2		2
Stock-based compensation									123		123
Exercise of common stock options							281		7		7
Net loss										(10,121)	(10,121)
BALANCE December 31, 2012	855,996	29,728	1,162,021	34,520			27,853	1		(64,720)	(64,719)
Issuance of Series C preferred stock, net of issuance costs of \$220 (unaudited)					8,142,891	56,780					
Issuance of Series C preferred stock, in redemption of bridge loan (unaudited)					428,526	3,000					
Accretion of preferred stock issuance costs (unaudited)		47		58		7			(112)		(112)
		962		1,305					(40)	(2,227)	(2,267)

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Accrued dividends (unaudited)												
Deemed contribution of preferred shareholders (unaudited)	(9,337)		(6,833)					16,170				16,170
Vesting of restricted common stock (unaudited)							15					
Repurchase of unvested restricted common stock (unaudited)								(5)				(5)
Stock-based compensation (unaudited)								153				153
Exercise of common stock options (unaudited)						225		11				11
Net loss (unaudited)										(11,799)		(11,799)
BALANCE September 30, 2013 (unaudited)	855,996	\$ 21,400	1,162,021	\$ 29,050	8,571,417	\$ 59,787	28,093	\$ 1	\$ 16,177	\$ (78,746)		\$ (62,568)

See notes to financial statements.

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Table of Contents**DICERNA PHARMACEUTICALS, INC.****Statements of Cash Flows**

For the years ended December 31, 2011 and 2012 and for the nine months ended September 30, 2012 and 2013

(In thousands)

	YEAR ENDED DECEMBER 31,		NINE MONTHS ENDED SEPTEMBER 30,	
	2011	2012	2012	2013
			<i>(Unaudited)</i>	
CASH FLOWS FROM OPERATING ACTIVITIES:				
Net loss	\$ (8,556)	\$ (10,121)	\$ (11,634)	\$ (11,799)
Adjustments to reconcile net loss to net cash used in operating activities:				
Deferred revenue	(1,908)	(1,014)	238	
Depreciation	474	551	412	392
Stock-based compensation	173	125	94	153
Loss on extinguishment of debt				318
Non-cash interest expense	32			
Amortization of debt discount	264	201	150	149
Amortization of debt issuance costs	90	24	18	18
Decrease in fair value of preferred stock warrant	(51)	(469)	(352)	(219)
Changes in operating assets and liabilities:				
Research and license receivable	(161)	(4,857)	156	5,018
Prepaid expenses and other current assets	61	28	7	97
Accounts payable	831	(216)	(668)	359
Accrued expenses and other current liabilities	(111)	49	36	248
Deferred rent	(4)	(38)	(24)	(49)
Net cash used in operating activities	(8,866)	(15,737)	(11,567)	(5,315)
CASH FLOWS FROM INVESTING ACTIVITIES				
Purchases of property and equipment	(501)	(120)	(120)	(192)
Net cash used in investing activities	(501)	(120)	(120)	(192)
CASH FLOWS FROM FINANCING ACTIVITIES:				
Proceeds from issuance of common stock	70	7		11
Repurchase of restricted common stock				(5)
Payments of deferred issuance costs				(173)
Proceeds from issuance of redeemable convertible preferred stock				57,000
Redeemable convertible preferred stock issuance costs				(220)
Proceeds from long-term debt	8,609			
Proceeds from bridge loan financing				3,000
Payments of long-term debt issuance costs	(47)			
Payments of long-term debt fees		(136)	(136)	
Repayments of long-term debt principal	(1,377)	(2,834)	(1,863)	(3,064)

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Net cash provided by (used in) financing activities	7,255	(2,963)	(1,999)	56,549
INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS	(2,112)	(18,820)	(13,686)	51,042
CASH AND CASH EQUIVALENTS Beginning of period	24,602	22,490	22,490	3,670
CASH AND CASH EQUIVALENTS End of period	\$ 22,490	\$ 3,670	\$ 8,804	\$ 54,712
NONCASH FINANCING ACTIVITIES:				
Accretion of redeemable convertible preferred stock	\$ 4,099	\$ 4,097	\$ 3,021	\$ 2,379
Deemed contribution of preferred shareholders	\$	\$	\$	\$ 16,170
Conversion of bridge loan financing	\$	\$	\$	\$ 3,000
Debt issuance costs issuance of Preferred stock warrants	\$ 477	\$	\$	\$
SUPPLEMENTAL CASH FLOW INFORMATION				
Cash paid for interest	\$ 578	\$ 1,123	\$ 1,007	\$ 624

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DICERNA PHARMACEUTICALS, INC.

Notes to Financial Statements

Information as of September 30, 2013 and for the nine months ended September 30, 2012 and 2013 is unaudited

(In thousands, except share and per share data)

1. Nature of Business and Basis of Presentation

Nature of business

Dicerna Pharmaceuticals, Inc. (the Company) is 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. The Company is using its proprietary RNA interference technology platform, which the Company believes improves on existing RNAi technologies, to build a broad pipeline in these therapeutic areas. The Company intends to discover, develop and commercialize novel therapeutics either on its own or in collaboration with pharmaceutical partners.

Basis of presentation

The Company continues to be subject to a number of risks common to companies in similar stages of development. Principal among these risks are the uncertainties of technological innovations, dependence on key individuals, development of the same or similar technological innovations by the Company's competitors and protection of proprietary technology. The Company's ability to fund its planned clinical operations, including completion of its planned trials, is expected to depend on the amount and timing of cash receipts under its existing collaboration agreement, as well as any future collaboration or product sales and/or financing transactions. In July 2013, the Company issued 8,142,891 shares of Series C mandatorily redeemable, convertible preferred stock (Series C) at an issuance price of \$7.00 per share for total gross proceeds of \$57,000 and issued 428,526 shares of Series C preferred stock in satisfaction of the \$3,000 bridge loan financing. The Series C preferred stock are convertible into common stock at an initial conversion rate of \$7.00 per share subject to adjustments for stock splits. The Series C preferred stock automatically convert to common stock upon occurrence of a qualified financing of more than \$60,000 of gross proceeds to the Company. The Series C preferred stock are mandatorily redeemable in three annual installments beginning no earlier than March 1, 2019.

Concurrent to the issuance of Series C preferred stock, the Company effected a reverse split of one-to-250 for its common stock and one-to-25 for its Series A and Series B preferred stock. All share and per share amounts related to common stock, preferred stock, stock options, warrants and restricted stock included in these financial statements have been restated to reflect the reverse stock split. The Company believes that its cash and cash equivalents of \$54,712 at September 30, 2013 (unaudited), combined with the change in redemption date of its Series A and B preferred stock disclosed in Note 9 will enable the Company to maintain its current and planned operations for the foreseeable future.

2. Summary of Significant Accounting Policies

Unaudited interim financial information

The accompanying balance sheet as of September 30, 2013, the statements of operations and statements of cash flows for the nine months ended September 30, 2012 and 2013 and the statement of redeemable convertible preferred stock and stockholders' deficit for the nine months ended September 30, 2013 are unaudited. The interim unaudited financial statements have been prepared on the same basis as the annual audited financial statements; and in the opinion of management, reflect all adjustments, which include only normal recurring adjustments necessary for the fair statement of the Company's financial position as of September 30, 2013, and the results of its operations and its cash flows for the nine months ended September 30, 2012 and 2013. The financial data and other information disclosed in these notes related to the nine months ended September 30, 2012 and 2013 are unaudited. The results for the nine months ended September 30, 2013 are not necessarily indicative of results to be expected for the year ending December 31, 2013, or any other interim periods, or any future year or period.

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DICERNA PHARMACEUTICALS, INC.

Notes to Financial Statements (continued)

2. Summary of Significant Accounting Policies (continued)

Unaudited pro forma financial information

On September 24, 2013, the Company's Board of Directors authorized the Company to file a registration statement with the Securities and Exchange Commission to sell shares of its common stock (the "Common Stock") to the public. The unaudited pro forma balance sheet as of September 30, 2013 assumes the automatic conversion of all the outstanding preferred stock into shares of Common Stock upon the completion of this proposed offering and the reclassification of the Company's outstanding warrants to purchase shares of Series A Redeemable Convertible Preferred Stock ("Series A"), Series B Redeemable Convertible Preferred Stock ("Series B") and Series C from a liability to equity, occurring upon the closing of the Company's proposed initial public offering (the "IPO").

Unaudited pro forma net income (loss) per share applicable to common stockholders is computed using the weighted-average number of common shares outstanding after giving effect to the conversion of all the outstanding redeemable convertible preferred stock into shares of Common Stock as if such conversion had occurred at the beginning of the period presented, or the date of original issuance, if later, and excludes the accretion to redemption value, accretion of dividends, net income available to preferred stockholders and the gain on extinguishment of preferred stock.

Significant estimates and judgments

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, and disclosure of contingent assets, and liabilities at the date of the financial statements and the reported amounts of license and research collaboration revenue and expenses during the reporting period. Actual results may differ from the Company's estimates. Significant estimates relied upon in preparing these financial statements include revenue recognition, the fair value of common stock, the fair value of preferred stock warrants, recoverability of the Company's net deferred tax assets and related valuation allowance and certain accruals. Actual results could differ materially from those estimates.

Cash equivalents

Cash equivalents include all highly liquid investments maturing within 90 days from the date of purchase. Cash equivalents consist of money market funds as of December 31, 2011 and 2012 and as of September 30, 2013 (unaudited), and are valued at cost, plus accrued interest, which approximates fair value.

Restricted cash

As of December 31, 2011 and 2012, and as of September 30, 2013 (unaudited), restricted cash represents a certificate of deposit that matures annually, and secures the Company's outstanding letter of credit of \$264 for the operating lease for office and laboratory space. The letter of credit is required to be maintained through the term of the lease, which was amended on July 3, 2013 to extend until November 30, 2016.

Concentrations of credit risk

Financial instruments that subject the Company to significant concentrations of credit risk consist of cash and cash equivalents and restricted cash. All of the Company's cash and cash equivalents and restricted cash are held at one financial institution that management believes to be of high credit quality. In addition, during 2011 and 2012, one counterparty accounted for all of the Company's revenue and research and license agreement receivable.

Deferred issuance costs

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Deferred issuance costs, which consist of direct incremental legal and professional accounting fees relating to the IPO, are capitalized. The deferred issuance costs will be offset against IPO proceeds upon the consummation of the offering. In the event the offering is terminated, deferred offering costs will be expensed. As of September 30, 2013 (unaudited), the Company capitalized \$173 of deferred IPO costs, which are included in prepaid expenses and other current assets on the balance sheet. No amounts were deferred as of December 31, 2011 or 2012.

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Table of Contents**DICERNA PHARMACEUTICALS, INC.****Notes to Financial Statements (continued)****2. Summary of Significant Accounting Policies (continued)*****Property and equipment***

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

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

Impairment of long-lived assets

Long-lived assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of the asset may not be recoverable. When such events occur, the Company compares the carrying amounts of the assets to their undiscounted expected future cash flows. If this comparison indicates that there is an impairment, the amount of the impairment is calculated as the difference between the carrying value and fair value of the related asset. For the years ended December 31, 2011 and 2012, and for the nine months ended September 30, 2013 (unaudited), no impairments have been recorded.

Fair value of financial instruments

The carrying amounts of the Company's financial instruments include cash equivalents, accounts payable, and other accrued expenses, approximate their fair values due to their short duration. Management believes that the Company's long-term debt bears interest at the prevailing market rate for instruments with similar characteristics and, accordingly, the carrying value of long-term debt also approximates their fair value.

Segment and geographic information

Operating segments are defined as components of an enterprise (business activity from which it earns revenue and incurs expenses) about which discrete financial information is available and regularly reviewed by the chief operating decision maker in deciding how to allocate resources and in assessing performance. The Company, through its Chief Executive Officer in his role as chief operating decision maker, views its operations and manages its business as one operating segment. All material long-lived assets of the Company are located in the United States.

Revenue recognition

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The Company generates revenue from research collaboration and license agreements with third parties which contain multiple deliverables. The deliverables in the agreements include (a) the use of the Company's technology and (b) research and development of product candidates. Such agreements may provide for consideration to the Company in the form of up-front payments, research and development services, milestone payments and royalties. Revenue is recognized when the following criteria have been met: (1) pervasive evidence of an arrangement exists; (2) delivery has occurred or services have been rendered and risk of loss has passed; (3) the seller's price to the buyer is fixed or determinable; and (4) collectability is reasonably assured. Multiple-deliverable arrangements 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.

At the inception of each arrangement that includes payments for optional research or milestones, the Company evaluates 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

Table of Contents**DICERNA PHARMACEUTICALS, INC.****Notes to Financial Statements (continued)****2. Summary of Significant Accounting Policies (continued)**

commensurate with either the entity's performance to achieve the milestone or the enhancement of the value of the delivered item(s); (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.

When the Company determines that an arrangement should be accounted for as a single unit of accounting, it must determine the period over which the performance obligations will be performed and revenue will be recognized. The Company's only revenue to date results from a research collaboration and license agreement entered into in December 2009. Non-refundable up-front license fees under the agreement were initially recorded as deferred revenue upon receipt and are being recognized as revenue over the Company's performance period as defined in the agreement. 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.

Royalty payments are recognized as revenue based on contract terms and reported sales of licensed products, when reported sales are reliably measurable and collectibility is reasonably assured.

Research and development costs

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

Preferred stock warrant liability

Freestanding warrants related to shares that are redeemable, contingently redeemable, or for purchases of preferred stock that are not indexed to the Company's own stock are classified as a liability on the Company's balance sheet. The warrants are recorded at fair value, estimated using the Black-Scholes option-pricing model, and marked to market at each balance sheet date with changes in the fair value of the liability recorded in the statements of operations. The Company classifies the liability as noncurrent as settlement is not expected within the next 12 months.

Redeemable convertible preferred stock

The Company initially records preferred stock that may be redeemed at the option of the holder or based on the occurrence of events not under the Company's 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, the Company adjusts the carrying value to the redemption value over the period from the issuance date to the earliest possible redemption date using the effective interest method. If it is not probable that the preferred stock will become redeemable, the Company does not adjust the carrying value. In the absence of retained earnings these accretion charges are recorded against additional paid-in-capital, if any, and then to accumulated deficit.

Common stock valuation

Due to the absence of an active market for the Company's common stock, the Company utilized methodologies in accordance with the framework of the American Institute of Certified Public Accountants Technical Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, to estimate the fair value of its common stock. In determining the exercise prices for options granted, the Company has considered the fair value of the common stock as of the measurement date. The fair value of the common stock has been determined at each award grant date based upon a variety of factors, including the illiquid nature of the common stock, arm's-length

Table of Contents**DICERNA PHARMACEUTICALS, INC.****Notes to Financial Statements (continued)****2. Summary of Significant Accounting Policies (continued)**

sales of the Company's capital stock (including redeemable convertible preferred stock), the effect of the rights and preferences of the preferred shareholders, and the prospects of a liquidity event. Among other factors are the Company's financial position and historical financial performance, the status of technological developments within the Company's research, the composition and ability of the current research and management team, an evaluation or benchmark of the Company's competition, and the current business climate in the marketplace. Significant changes to the key assumptions underlying the factors used could result in different fair values of common stock at each valuation date.

Stock-based compensation

The Company accounts for share-based payments at fair value, which is measured using the Black-Scholes option pricing model. The fair value measurement date for employee awards is generally the date of grant. The fair value measurement date for nonemployee awards is generally the date the performance of services is completed. Share-based compensation costs are recognized as expense over the requisite service period, which is generally the vesting period, on a straight-line basis for all time-vested awards.

Share-based payments to nonemployees are remeasured at each reporting date and recognized as services are rendered, generally on a straight-line basis. The Company believes that the fair value of these awards is more reliably measurable than the fair value of the services rendered.

Income taxes

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

The Company also assesses the probability that the positions taken or expected to be taken in its income tax returns will be sustained by taxing authorities. A more likely than not (more than 50 percent) recognition threshold must be met before a tax benefit can be recognized. Tax positions that are more likely than not to be sustained are reflected in the Company's financial statements. Tax positions are measured as the largest amount of tax benefit that is greater than 50 percent likely of being realized upon settlement with a taxing authority that has full knowledge of all relevant information. The difference between the benefit recognized for a position and the tax benefit claimed on a tax return is referred to as an unrecognized tax benefit. Potential interest and penalties associated with such uncertain tax positions are recorded as a component of income tax expense. At December 31, 2011 and 2012, and at September 30, 2013 (unaudited), the Company had not identified any significant uncertain tax positions.

Loss per share and unaudited pro forma loss per share

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

Table of Contents**DICERNA PHARMACEUTICALS, INC.****Notes to Financial Statements (continued)****2. Summary of Significant Accounting Policies (continued)*****Comprehensive loss***

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

Guarantees and indemnifications

The Company is not a guarantor under any agreements.

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

Through December 31, 2012, and for the nine months ended September 30, 2013 (unaudited), the Company had not experienced any losses related to this indemnification obligation and no claims with respect thereto were outstanding. The Company does not expect material claims related to this indemnification obligation, and consequently, concluded that the fair value of this obligation is negligible and no related liabilities were established.

The Company has indemnified, under pre-determined conditions and limitations, a counterparty for infringement of third-party intellectual property rights by the Company. The Company does not believe, based on information available, that it is probable that any material amounts will be paid under these indemnification provisions.

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

3. Net Loss Per Share Attributable to Common Stockholders

The following table summarizes the computation of basic and diluted net loss per share attributable to common stockholders of the Company (in thousands, except share and per share data):

	YEARS ENDED DECEMBER 31,		NINE MONTHS ENDED SEPTEMBER 30,	
	2011	2012	2012	2013
			<i>(Unaudited)</i>	
Net loss	\$ (8,556)	\$ (10,121)	\$ (11,634)	\$ (11,799)
Accretion of preferred stock issuance costs to redemption value	(63)	(61)	(47)	(112)
Accrued dividends on preferred stock	(4,036)	(4,036)	(3,021)	(2,267)
Net loss attributable to common stockholders - basic and diluted	\$ (12,655)	\$ (14,218)	\$ (14,702)	\$ (14,178)
Weighted-average number of common shares - basic and diluted	25,682	27,554	27,539	28,050
Net loss per share attributable to common stockholders - basic and diluted	\$ (492.76)	\$ (516.00)	\$ (533.86)	\$ (505.45)

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Table of Contents**DICERNA PHARMACEUTICALS, INC.****Notes to Financial Statements (continued)****3. Net Loss Per Share Attributable to Common Stockholders (continued)**

The following potentially dilutive securities outstanding, prior to the use of the treasury stock method or if-converted method, have been excluded from the computation of diluted weighted-average common shares outstanding, because such securities had an anti-dilutive impact due to the losses reported:

	AS OF			
	DECEMBER 31, 2011	2012	2012	SEPTEMBER 30, 2013
			<i>(Unaudited)</i>	
Options to purchase common stock	26,982	25,512	25,332	42,127
Warrants to purchase common stock	2,198	2,198	2,198	2,198
Warrants to purchase redeemable convertible preferred stock	22,157	47,400	47,400	77,537
Redeemable convertible preferred stock	2,018,017	2,018,017	2,018,017	4,444,333
Unvested restricted stock	231	152	158	7

The unaudited pro forma basic and diluted loss per share attributable to common stockholders for the year ended December 31, 2012 and the nine months ended September 30, 2013 give effect to the automatic conversion of all shares of redeemable convertible preferred stock upon an IPO by treating all shares of redeemable convertible preferred stock as if they had been converted to common stock in all periods in which such shares were outstanding. Accordingly, the pro forma basic and diluted loss per share attributable to common stockholders do not include the effects of the accretion of redeemable convertible preferred stock to redemption value and accretion of dividends. Shares to be sold in the offering are excluded from the unaudited pro forma basic and diluted loss per share attributable to common stockholders calculations.

As the Company incurred net losses for the year ended December 31, 2012 and the nine months ended September 30, 2013 (unaudited), there is no income allocation required under the two-class method or dilution attributed to pro forma weighted average shares outstanding in the calculation of pro forma diluted loss per share attributable to common stockholders.

Unaudited pro forma basic and diluted loss per share attributable to common stockholders are computed as follows (in thousands, except share and per share data):

YEAR ENDED DECEMBER 31,	NINE MONTHS ENDED SEPTEMBER 30,
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	2012	2013
		<i>(unaudited)</i>
Pro forma loss per share basic and diluted		
Numerator:		
Net loss attributable to common stockholders basic and diluted	\$ (14,218)	\$ (14,178)
Add: accretion of preferred stock issuance costs to redemption value	61	112
Add: accrued dividends on redeemable convertible preferred stock	4,036	2,267
Net loss	\$ (10,121)	\$ (11,799)
Denominator:		
Weighted average number of shares outstanding basic and diluted	27,554	28,050
Add: adjustment to reflect assumed effect of conversion of redeemable convertible preferred stock	2,018,017	4,416,283
Pro forma weighted average number of shares outstanding basic and diluted	2,045,571	4,444,333
Pro forma net loss per share basic and diluted	\$ (4.95)	\$ (2.65)

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Table of Contents**DICERNA PHARMACEUTICALS, INC.****Notes to Financial Statements (continued)****4. Prepaid Expenses and Other Current Assets**

Prepaid expenses and other current assets consists of the following:

	DECEMBER 31, 2011	2012	SEPTEMBER 30, 2013 <i>(unaudited)</i>
Prepaid expenses	\$ 312	\$ 290	\$ 222
Debt issuance costs	24	24	18
Deferred IPO costs			173
Other current assets	36	30	
Prepaid expenses and other current assets	\$ 372	\$ 344	\$ 413

5. Property and Equipment, Net

Property and equipment, net consists of the following:

	DECEMBER 31, 2011	2012	SEPTEMBER 30, 2013 <i>(unaudited)</i>
Office and computer equipment	\$ 212	\$ 224	\$ 229
Laboratory equipment	1,903	2,010	2,019
Furniture and fixtures	233	233	265
Leasehold improvements	288	289	435
Property and equipment at cost	2,636	2,756	2,948
Less accumulated depreciation	(1,322)	(1,873)	(2,265)
Property and equipment net	\$ 1,314	\$ 883	\$ 683

Depreciation expense for the years ended December 31, 2011 and 2012 and for the nine months ended September 30, 2012 (unaudited) and 2013 (unaudited) was \$474, \$551, \$412 and \$392, respectively.

6. Long-term Debt

On March 26, 2009, the Company entered into a loan and security agreement with an independent finance company, Hercules Technology II, LP (Hercules), for up to \$7,000 and drew down the total proceeds in three separate advances between March 2009 and September 2009. The original agreement called for the Company to repay such borrowings over a 36-month period, including interest at a variable annual rate not less than 10.15% and not to exceed 12.75%. The loan is collateralized by a security interest in all tangible assets. In addition, the Company is subject to certain financial reporting requirements and certain negative covenants requiring lender consent. On May 28, 2010, the Company and Hercules executed an amendment to the loan and security agreement to defer \$653 in principal payments originally due in June 2010 through August 2010, and amortized such deferred principal amounts equally over the remaining payment term beginning in September 2010. On June 28, 2011, the Company and Hercules executed a second amendment to the loan and security agreement, which increased the maximum loan amount to \$12,000. Upon execution of the second amendment, the Company drew a \$7,000 advance, a portion of which the Company used to repay the outstanding balance of principal and interest under the original loan and security agreement. On December 15, 2011, the Company drew down the remaining \$5,000. Interest is payable monthly and principal is to be repaid in equal monthly installments beginning April 1, 2012

Table of Contents**DICERNA PHARMACEUTICALS, INC.****Notes to Financial Statements (continued)****6. Long-term Debt (continued)**

through January 2, 2015. The applicable annual interest rate was 10.15% at December 31, 2011 and 2012 and at September 30, 2012 (unaudited) and 2013 (unaudited), respectively.

In connection with the advances under the original loan and security agreement, the Company issued warrants to the lender for the purchase of an aggregate of 21,000 shares of the Company's Series A at an exercise price of \$25.00 per share. With the advances under the second amendment to the loan and security agreement, the Company issued warrants for the purchase of an aggregate of 26,400 shares of the Company's Series B at an exercise price of \$25.00 per share. The warrants are immediately exercisable and expire 10 years from the date of grant. The fair value of the warrants were recorded as discounts to the debt and are being amortized to interest expense using the effective interest method over the loan repayment term. The warrants are classified as a liability in the accompanying balance sheets. The Company estimated the issuance date fair value of the 26,400 warrants granted in 2011 to be \$477. The issuance date fair value was determined using the Black-Scholes option-pricing model with the following assumptions: risk-free interest rate of approximately 2.5%, expected life of 10 years, volatility of 64%, and no expected dividends.

The estimated fair value of the outstanding warrants at December 31, 2011 and 2012 and at September 30, 2013 (unaudited), was \$800, \$331 and \$117, respectively. The fair value was determined using the Black-Scholes option-pricing model with the following assumptions:

	DECEMBER 31,	DECEMBER 31,	SEPTEMBER 30,
	2011	2012	2013
			<i>(unaudited)</i>
Expected option term (in years)	7 to 9	6 to 8	5 to 8
Expected volatility	64%	66%	66%
Risk-free interest rate	2.0	1.7	2.8
Expected dividend yield	0.00%	0.00%	0.00%

The adjustment to the preferred stock warrant liability was recorded in other income and for the years ended December 31, 2011 and 2012 and for the nine months ended September 30, 2012 (unaudited) and 2013 (unaudited) amounted to \$51, \$469, \$234 and \$214, respectively.

At December 31, 2012, the principal maturities of the debt were as follows:

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2013	\$ 4,140
2014	4,587
2015	439
Principal balance outstanding December 31, 2012	9,166
Less: unamortized discount	(366)
Less: current portion	(4,140)
Long-term debt outstanding	\$ 4,660

7. Bridge Loan Financing

On June 26, 2013, the Company issued convertible notes and warrants for the purchase of preferred stock in the next qualified financing to existing preferred and common shareholders for approximately \$3,000 (bridge loan financing). The notes mature on June 26, 2018, unless previously converted or repaid. In the event the Company

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DICERNA PHARMACEUTICALS, INC.

Notes to Financial Statements (continued)

7. Bridge Loan Financing (continued)

obtains financing through the issuance of equity securities, including an IPO, prior to the maturity date, the notes automatically convert into shares of the equity issued in such a qualified financing and at the lowest price per share of the equity securities issued and sold in that financing. If a liquidation event occurs prior to June 26, 2018, the notes can be converted at the option of the holder for an amount equal to two times the outstanding principal balance of the notes in cash or the issuance of Series B preferred stock equal to the outstanding principal balance of the notes divided by 0.9. The notes have an interest rate of 7% per year, payable at the earlier of the notes' conversion or maturity.

The purpose of this bridge loan financing was to provide operating cash to the Company until it completed the issuance of the Series C in July 2013, at which time the notes were converted into 428,526 shares of Series C preferred shares at \$7.00 per share and the related accrued interest of \$20 became payable.

In connection with the issuance of the bridge loan financing, the Company issued warrants for the purchase of an aggregate of 85,703 shares of the Company's preferred stock in the next qualified financing at an exercise price of \$7.00 per share. The warrants are immediately exercisable and expire 5 years from the date of issuance. The Company estimated the fair value of the warrants at the date of issuance to be \$324. The fair value of the warrants was recorded as a discount to the convertible notes upon issuance, and is classified as a liability in the accompanying balance sheet. The issuance date fair value was determined using the Black-Scholes option-pricing model with the following assumptions: risk-free interest rate of approximately 1.2%, expected life of 5 years, volatility of 64%, and no expected dividends. The estimated fair value of the outstanding warrants at September 30, 2013 (unaudited) was \$319, using the Black-Scholes option-pricing model with the following assumptions: risk-free interest rate of approximately 1.6%, expected life of 4.7 years, volatility of 64%, and no expected dividends. The adjustment to the preferred stock warrant liability was recorded in other income and for the nine months ended September 30, 2013 (unaudited) amounted to \$5.

The bridge loan discount was amortized to interest expense using the effective interest method over the loan repayment term, and the unamortized discount of \$318 was reflected as a loss on extinguishment of the bridge loan in the accompanying statement of operations (unaudited), when the notes were converted to Series C in July 2013.

8. Revenue

In December 2009, the Company entered into a research collaboration and license agreement with Kyowa Hakko Kirin Co., Ltd. (KHK) for the research, development and commercialization of drug delivery systems and DsiRNA pharmaceuticals for therapeutic targets primarily in oncology. The Company granted KHK an exclusive, worldwide, royalty-bearing and sub-licensable license to the DsiRNA and drug delivery technologies and intellectual property for certain selected DsiRNA-based compounds. Under the agreement, KHK is responsible for activities to develop, manufacture and commercialize the selected DsiRNA-based compounds and pharmaceutical products containing such compounds.

Since the initiation of the research collaboration and license agreement two target programs, including the initial target KRAS, have been nominated by KHK for formal development studies. Both target programs utilize the Company's specific RNAi-inducing double-stranded DsiRNA molecules and a lipid nanoparticle drug delivery system proprietary to KHK.

The Company is entitled to receive up to \$110,000 in regulatory, clinical and commercialization milestone payments, and royalties on net sales of each product candidate under the KHK agreement.

The deliverables at the effective date of the agreement include delivery of intellectual property, conducting the KRAS research and development program, and providing KHK the exclusive option right to reserve additional targets. The Company concluded the performance of additional research for each additional target, if exercised by KHK, is not a deliverable of the agreement at inception because it is a substantive option and is not priced at a significant and incremental discount.

Table of Contents**DICERNA PHARMACEUTICALS, INC.****Notes to Financial Statements (continued)****8. Revenue (continued)**

The performance period is the expected period over which the services of the combined unit are performed which spans from the contract inception through the end of 2011. The Company received cash payments of \$5,500, \$6,000, \$1,000 and \$5,000 in 2010, 2011, 2012 and 2013, respectively, under the research collaboration and license agreement with KHK, which amounts included license fees, option exercise fees and research funding.

The Company has no further obligations under the research collaboration and license agreement related to the KRAS target or the additional target.

The Company recognized option and milestone payments of \$5,408, \$7,015, \$762 and none in 2011 and 2012 and for the nine months ended September 30, 2012 (unaudited) and 2013 (unaudited), respectively, related to the exercise of substantive options and milestones when the milestone and options were achieved and performance related to such milestones was completed.

As of December 31, 2011 the Company had deferred revenue of \$1,014 related to this agreement.

9. Redeemable Convertible Preferred Stock

The Company has issued Series A, Series B and Series C redeemable convertible preferred stock (collectively, the Preferred Stock). The Company classifies the Preferred Stock outside of stockholders' deficit because the stocks contain redemption features that are not solely within the Company's control.

Preferred Stock consisted of the following as of December 31, 2011:

	PREFERRED STOCK AUTHORIZED	ISSUANCE DATES	PREFERRED STOCK ISSUED AND OUTSTANDING	REDEMPTION VALUE/ LIQUIDATION PREFERENCE	CARRYING VALUE	COMMON STOCK ISSUABLE UPON CONVERSION
Series A	880,000	April 2007	9,999			
		July 2007	19,999			
		November 2007	489,999			
		July 2008	335,999			
			855,996	\$ 28,063	\$ 27,990	855,996
Series B	1,190,000	August 2010	992,021			
		September 2010	10,000			
		October 2010	160,000			
			1,162,021	32,254	32,161	1,162,021

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Total	2,070,000	2,018,017	\$	60,317	\$	60,151	2,018,017
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Table of Contents**DICERNA PHARMACEUTICALS, INC.****Notes to Financial Statements (continued)****9. Redeemable Convertible Preferred Stock (continued)**

Preferred Stock consisted of the following as of December 31, 2012:

	PREFERRED STOCK AUTHORIZED	ISSUANCE DATES	PREFERRED STOCK ISSUED AND OUTSTANDING	REDEMPTION VALUE/ LIQUIDATION PREFERENCE	CARRYING VALUE	COMMON STOCK ISSUABLE UPON CONVERSION
Series A	880,000	April 2007	9,999			
		July 2007	19,999			
		November 2007	489,999			
		July 2008	335,999			
			855,996	\$ 29,775	\$ 29,728	855,996
Series B	1,190,000	August 2010	992,021			
		September 2010	10,000			
		October 2010	160,000			
			1,162,021	34,578	34,520	1,162,021
Total	2,070,000		2,018,017	\$ 64,353	\$ 64,248	2,018,017

Preferred Stock consisted of the following as of September 30, 2013 (unaudited):

	PREFERRED STOCK AUTHORIZED	ISSUANCE DATES	PREFERRED STOCK ISSUED AND OUTSTANDING	REDEMPTION VALUE/ LIQUIDATION PREFERENCE	CARRYING VALUE	COMMON STOCK ISSUABLE UPON CONVERSION
Series A	880,000	April 2007	9,999			

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		July 2007	19,999			
		November 2007	489,999			
		July 2008	335,999			
			855,996	\$	21,400	\$ 21,400 855,996
Series B	1,190,000	August 2010	992,021			
		September 2010	10,000			
		October 2010	160,000			
			1,162,021		29,050	29,050 1,162,021
Series C	9,000,000	July 2013	8,571,417		60,000	59,787 8,571,417
Total	11,070,000		10,589,434	\$	110,450	\$ 110,237 10,589,434

The Series A, Series B and Series C preferred stock has the following rights and preferences:

Voting

The holders of Series A, Series B and Series C are entitled to one vote per common share equivalent on all matters voted on by holders of common stock.

Dividends

The holders of Series A and Series B are entitled to receive cumulative dividends at the rate of \$2.00 per share per annum in preference to any dividends on common stock, payable only when and if declared by the Board of Directors. Dividends accrue daily in arrears and are not compounded, whether or not declared by the Board of Directors. As of December 31, 2012, the Company has accrued \$13,903 in cumulative dividends; no dividends have been declared.

Table of Contents**DICERNA PHARMACEUTICALS, INC.****Notes to Financial Statements (continued)****9. Redeemable Convertible Preferred Stock (continued)**

Concurrent with the July 2013 Series C financing, the Series A and Series B dividends only will accrue if declared by the Board of Directors. If declared, the holders of Series C preferred stock are entitled to accrue dividends at the rate of \$0.56 per share per annum in preference to any dividends on Series A, Series B or common stock.

Liquidation rights

In the event of any liquidation, dissolution or winding-up of the Company, the Series A and Series B rank senior to the Company's common stock and the holders of Series A and Series B preferred stocks shall be entitled to receive their original purchase price together with all accumulated but unpaid dividends prior to any distributions being made to common stock. Upon completion of the payment of principal and declared but unpaid dividends to the holders of Series A and Series B preferred stocks, all of the remaining assets shall be distributed among the holders of Series A and Series B and common stock pro rata based on the number of shares of common stock held by each, assuming full conversion of all outstanding shares of Series A and Series B preferred stocks. In the event of any liquidation, dissolution or winding-up of the Company, the Series C rank senior to the Series A and Series B and the holders of Series C shall be entitled to receive their original purchase price together with all accumulated but unpaid dividends prior to any distributions being made to Series A and Series B.

Conversion

Each Series A and Series B preferred stock is convertible at the option of the holder at any time after issuance into the number of fully paid and nonassessable shares of common stock as determined by dividing the original issuance price of \$25.00 per stock, plus any declared and unpaid dividends thereon by the conversion price in effect on the date the certificate is surrendered for conversion. The initial conversion price is \$25.00 per stock and is subject to adjustment for certain dilutive events, as defined. Each Series A and Series B preferred stock will automatically be converted into one share of common stock in the event of an initial public offering that results in minimum net proceeds to the Company of \$30,000 or at the election of the holders of at least 60% of the then outstanding Series A and Series B preferred stock. Each share of Series C is convertible at the option of the holder at any time after issuance into the number of fully paid and nonassessable shares of common stock as determined by dividing the original issuance price of \$7.00 per share, plus any declared and unpaid dividends thereon by the conversion price in effect on the date the certificate is surrendered for conversion. The initial conversion price is \$7.00 per share and is subject to adjustment for certain dilutive events, as defined. In July 2013, the terms of the Series A, Series B and Series C were amended such that each share of Series A, Series B and Series C will automatically be converted into one share of common stock in the event of an initial public offering that results in minimum net proceeds to the Company of \$60,000 or at the election of the holders of at least a majority of the then outstanding shares of preferred stock, the majority of which includes at least 74% of the holders of the then outstanding shares of Series C.

Redemption

At any time on or after April 1, 2015, and at the request of the holders of not less than 60% of the then outstanding Series A and Series B preferred stock, the Company will redeem all of the then outstanding Series A and Series B preferred stock at an amount equal to the original issue price, plus all accumulated but unpaid dividends on such Series A and Series B preferred stock in three equal annual installments beginning on the redemption date.

The Company is accreting the carrying value of Series A and Series B preferred stock to redemption value over the period from issuance to the earliest redemption date of April 1, 2015. The accretion amounts are recorded as an increase to the carrying value of the Series A and Series B preferred stock with a corresponding charge to additional paid-in capital, if any, and then to accumulated deficit.

Concurrent with the July 2013 issuance of Series C preferred stocks, the Series A and Series B redemption date was extended to March 1, 2019. At any time on or after March 1, 2019 and at the request of the holders of at least a majority of the then outstanding shares of preferred stock, the majority of which includes at least 74% of the holders of the then outstanding shares of Series C, the Company will redeem all of the then outstanding shares of preferred

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DICERNA PHARMACEUTICALS, INC.

Notes to Financial Statements (continued)

9. Redeemable Convertible Preferred Stock (continued)

stock at an amount equal to the original issue price, plus all accruing dividends declared but unpaid on such shares of preferred stock in three equal annual installments beginning on the redemption date.

Modification of Series A and Series B rights and preferences

The aforementioned modification of the Series A and Series B rights and preferences was reflected as a deemed contribution by the Series A and Series B preferred shareholders of their forfeited rights to the accrued dividends on the modification date. On July 25, 2013, the carrying amount of the Series A and Series B preferred stock immediately preceding the modification included \$16,170 of accrued dividends. The resulting deemed contribution was recorded as a \$16,170 increase to additional paid-in capital in the accompanying financial statements (unaudited).

10. Common Stock and Stock Option Plan

Common stock

Voting, dividend and liquidation rights of the holders of the common stock are subject to and qualified by the rights, powers and preferences of the holders of the preferred stock.

Voting

The holders of the common stock are entitled to one vote for each share of common stock held at all meetings of stockholders. The number of authorized shares of common stock may be increased or decreased (but not below the number of shares thereof) by the affirmative vote of the holders of shares of capital stock of the Company representing a majority of the votes represented by all outstanding shares of capital stock of the Company entitled to vote.

Dividends

Subject to the payment in full of all preferential dividends to which the holders of the preferred stock are entitled, the holders of common stock shall be entitled to receive dividends out of funds legally available therefor at such times and in such amounts as the Board of Directors of the Company may determine in its sole discretion, with holders of preferred stock and common stock sharing *pari passu* in such dividends.

Liquidation

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company, after the payment or provision for payment of all debts and liabilities of the Company and all preferential amounts to which the holders of preferred stock are entitled with respect to the distribution of assets in liquidation, the holders of common stock shall be entitled to share ratably in the remaining assets of the Company available for distribution.

Stock option plan

On July 1, 2007, the Board of Directors approved the 2007 Employee, Director, and Consultant Stock Plan, which provides for the grant of qualified incentive stock options, nonqualified stock options, and restricted stock to employees, directors, and nonemployees. On May 5, 2010, the Board of Directors approved the Fourth Amended and Restated 2007 Employee, Director, and Consultant Stock Plan, which authorizes further issuances of up to 30,254 shares of the Company's common stock. On October 14, 2010, the Board of Directors approved the termination of the 2007 Employee, Director and Consultant Stock Plan and adopted the 2010 Employee Director and Consultant Equity Incentive Plan (the 2010 Plan). The 2010 Plan, as adopted, authorizes further issuances of up to 45,214 shares of the Company's common stock. On February 9, 2012, the Board of Directors approved an amendment to the 2010 Plan to increase the number of shares authorized for purchase by 4,800 shares,

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thereby providing for the purchase of up to 49,014 shares of the Company's common stock. On July 30, 2013, the Board of Directors approved an amendment to the 2010 Plan to increase the number of shares authorized for purchase by 1,715,851 shares, thereby providing for the purchase of up to 1,764,865 shares of the Company's common stock. The stock options generally vest 25% after 12 months, followed by ratable vesting over 36 months and expire 10 years from the grant date.

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Table of Contents**DICERNA PHARMACEUTICALS, INC.****Notes to Financial Statements (continued)****10. Common Stock and Stock Option Plan (continued)**

Stock-based compensation expense is classified in the statements of operations as follows:

	YEAR ENDED DECEMBER 31,		NINE MONTHS ENDED SEPTEMBER 30,	
	2011	2012	2012	2013 <i>(unaudited)</i>
Research and development	\$ 52	\$ 14	\$ 13	\$ 33
General and administrative	121	111	81	120
Total	\$ 173	\$ 125	\$ 94	\$ 153

The fair value of each stock option award is estimated on the date of grant using the Black-Scholes option-pricing model that uses the assumptions noted in the table below. Expected volatility for the Company's common stock was determined based on an average of the historical volatility of a peer group of similar companies. The Company has limited stock option exercise information, as such; the expected term of stock options granted was calculated using the simplified method, which represents the average of the contractual term of the stock option and the weighted-average vesting period of the stock option. The assumed dividend yield is based upon the Company's expectation of not paying dividends in the foreseeable future. The risk-free rate for periods within the expected life of the stock option is based upon the U.S. Treasury yield curve in effect at the time of grant.

The assumptions used in the Black-Scholes option-pricing model for stock options granted during the years ended December 31, 2011 and 2012 are as follows:

	DECEMBER 31,	
	2011	2012
Expected option term (in years)	6	6
Expected volatility	58%	64%
Risk-free interest rate	0.9%	0.7%
Expected dividend yield	0.00%	0.00%

Using the Black-Scholes option-pricing model, the weighted-average grant date fair value of stock options granted during the years ended December 31, 2011 and 2012 and the nine months ended September 30, 2012 (unaudited) and 2013 (unaudited) was \$27.50, \$30.00, \$30.00 and \$2.01 per share, respectively. As of December 31, 2012 and September 30, 2013 (unaudited), there was \$239 and \$2,577, respectively, of unrecognized compensation cost related to nonvested employee and nonemployee stock option grants under the 2010 Plan which is expected to be recognized over a weighted-average period of seventeen months and twenty-two months, respectively. The weighted average assumptions in the Black-Scholes option-pricing model for stock options granted during the nine months ended September 30, 2012 and 2013 are as follows: risk-free interest rate of 0.7% and 1.6%, volatility of 64% and 64%, estimated life of approximately 6 years, and no expected dividends. The total intrinsic value of stock options exercised during the year ended December 31, 2011 was \$51. During the year ended December 31, 2012 and the nine months ended September 30, 2013 (unaudited), there was no intrinsic value for stock options exercised. There were no stock options exercised during the nine months ended September 30, 2012 (unaudited). Cash received from stock option exercises for the years ended December 31, 2011 and 2012 and the nine months ended September 30, 2013 (unaudited) was \$60, \$7 and \$11, respectively.

On September 24, 2013, the Board of Directors approved the repricing of all of the then outstanding 24,811 stock options, with an original per-share weighted average exercise price of \$45.16, to a new per-share exercise price of \$3.42, which represented the current per-share fair market value of common stock. The repricing was treated by the

Table of Contents**DICERNA PHARMACEUTICALS, INC.****Notes to Financial Statements (continued)****10. Common Stock and Stock Option Plan (continued)**

Company as an exchange of the original awards for new awards, with the incremental fair value of the new awards over the fair value of the old awards measured as of the modification date. Based upon this accounting treatment, the incremental fair value of \$30 was partially recognized in the nine months ended September 30, 2013, in the amount of \$23 (unaudited), representing the value of vested awards. The remaining \$7 (unaudited) will be recognized over the remaining vesting period of the awards.

Stock options granted to nonemployees

Stock-based compensation expense related to stock options granted to nonemployees is recognized as the consulting services are rendered, generally on a straight-line basis. The Company believes that the fair value of the stock options is more reliably measurable than the fair value of the services received. Compensation expense is subject to remeasurement until the options vest.

The Company granted options for 100 shares of common stock to nonemployees with an initial fair value of \$4 in 2011. There were no such grants in 2012. In the nine months ended September 30, 2013 (unaudited), the Company granted options for 132,500 shares of common stock to nonemployees with an initial fair value of \$337. The Company has recorded stock-based compensation expense of \$6 and a stock-based compensation credit of \$19 during the years ended December 31, 2011 and 2012, respectively, which is included in the total stock-based compensation expense of \$173 and \$125 for 2011 and 2012, respectively. Compensation expense is subject to remeasurement until the stock options vest. The assumptions used to estimate fair value were as follows: risk-free interest rate of 2.0%, 1.7%, and 2.8% as of December 31, 2011 and 2012 and as of September 30, 2013 (unaudited), respectively, volatility of 64% and 66%, as of December 31, 2011 and as of December 31, 2012 and as of September 30, 2013 (unaudited), respectively, remaining contractual life of approximately 7 years, and no expected dividends in 2011 and 2012 and for the nine months ended September 30, 2013 (unaudited).

A summary of stock option activity for employee and nonemployee awards under the Plan are presented below:

	NUMBER OF OPTIONS	WEIGHTED- AVERAGE EXERCISE PRICE PER SHARE	WEIGHTED- AVERAGE REMAINING CONTRACTUAL TERM (YEARS)
OUTSTANDING January 1, 2012	23,661	\$ 45.00	8.3
Granted	3,380	50.00	
Exercised	(281)	25.00	
Forfeited	(1,073)	47.50	
OUTSTANDING December 31, 2012	25,687	45.00	8.0
EXERCISABLE December 31, 2012	14,519	42.50	7.1
Vested and expected to vest as of December 31, 2012	24,029	45.00	7.5

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OUTSTANDING January 1, 2013	25,687	45.00	8.0
Granted (unaudited)	1,401,000	3.42	
Exercised (unaudited)	(225)	50.00	
Forfeited (unaudited)	(651)	50.00	
OUTSTANDING September 30, 2013 (unaudited)	1,425,811	3.42	9.9
EXERCISABLE September 30, 2013 (unaudited)	82,315	3.42	9.2
Vested and expected to vest as of September 30, 2013 (unaudited)	1,228,879	\$ 3.42	9.9

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Table of Contents**DICERNA PHARMACEUTICALS, INC.****Notes to Financial Statements (continued)****10. Common Stock and Stock Option Plan (continued)**

Under the Company's 2007 and 2010 stock option plans, as amended, the Company has reserved 1,747,164 shares of common stock for future issuance at December 31, 2012.

Restricted stock

During 2007, the Company issued a total of 320 shares of the Company's common stock to a scientific advisor of the Company as consideration for services. The fair value of these shares was \$8 at the issuance date. The shares, prior to vesting, are subject to repurchase and transfer restrictions that lapsed in November 2011. As of December 31, 2011 and 2012, there are no remaining shares subject to repurchase. The Company has recorded stock-based compensation expense of \$4 and \$3 in 2011 and 2012, respectively, associated with the vesting of these shares. In June 2011, the Company issued 200 shares of the Company's common stock to a scientific advisor of the Company at a purchase price of \$50.00 per share. The fair value of these shares was \$10 at the vesting date. The shares, prior to vesting, are subject to repurchase and transfer restrictions that lapse ratably over 48 months beginning in July 2011. As of December 31, 2012, there are 125 shares subject to repurchase at \$50.00 per share. In addition, if the scientific advisor ceases to be affiliated with the Company, the Company has the option to repurchase any unvested shares from the scientific advisor at the issuance price per share. In July 2013, the Company repurchased 100 unvested shares from the scientific advisor at a price of \$50.00 per share.

As of December 31, 2012, there was no unrecognized compensation cost related to restricted stock.

A summary of the Company's restricted stock is presented below:

	SHARES	WEIGHTED- AVERAGE GRANT DATE FAIR VALUE PER SHARE
Nonvested January 1, 2012	175	\$ 50
Vested	(50)	50
Nonvested December 31, 2012	125	50
Vested (unaudited)	(25)	50
Repurchased (unaudited)	(100)	50

Nonvested September 30, 2013 (unaudited)

11. Fair Value Measurements

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

The Company's cash equivalents are measured at fair value on a recurring basis and classified within Level 1 of the fair value hierarchy because they are valued using quoted market prices for the years ended December 31, 2011 and 2012, and for the nine months ended September 30, 2013 (unaudited).

Table of Contents**DICERNA PHARMACEUTICALS, INC.****Notes to Financial Statements (continued)****11. Fair Value Measurements (continued)**

The fair value of restricted cash, accounts payable, and accrued expenses approximate their carrying value due to the short maturity of these instruments and are classified within Level 2 of the fair value hierarchy. The Company's long-term debt and bridge loan financing bear interest at the prevailing market rates for instruments with similar characteristics and, accordingly, the carrying value for these instruments also approximate their fair value and are also classified within Level 2 of the fair value hierarchy.

The fair value of the preferred stock warrant liability, which is classified within Level 3, was determined using the Black-Scholes option-pricing model, for the years ended December 31, 2011 and 2012, and for the nine months ended September 30, 2013 (unaudited).

The following table provides a roll-forward of the Company's liabilities measured at fair value on a recurring basis using unobservable inputs (Level 3):

BALANCE January 1, 2011	\$ 374
Issuance of preferred stock warrants	477
Change in fair value of warrant liability	(51)
 BALANCE December 31, 2011	 800
Change in fair value of warrant liability	(469)
 BALANCE December 31, 2012	 331
Issuance of preferred stock warrants (unaudited)	324
Change in fair value of warrant liability (unaudited)	(219)
 BALANCE September 30, 2013 (unaudited)	 \$ 436

The preferred stock warrant liability will increase or decrease each period based on the fluctuations of the fair value of the underlying preferred stock. A significant fluctuation in the preferred stock fair value would not result in a material increase or decrease in the fair value of the preferred stock warrant liability.

12. Income Taxes

The Company had no current or deferred income tax expense for the years ended December 31, 2011 and 2012 due to its net operating loss position. The Company did not record a federal or state income tax provision or benefit for the nine months ended September 30, 2012 (unaudited) and 2013 (unaudited) due to the losses incurred in the corresponding periods as well as the Company's continued maintenance of a full valuation allowance against its net deferred tax assets.

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

	YEAR ENDED	
	DECEMBER 31, 2011	DECEMBER 31, 2012
Federal statutory rate	34.0%	34.0%
Effect of:		
Change in valuation allowance	(37.9)	(33.2)
Research and development tax credit	3.9	(1.9)
Stock-based compensation	(0.6)	(0.4)
Other	0.6	1.5
Total	0.0%	0.0%

Table of Contents**DICERNA PHARMACEUTICALS, INC.****Notes to Financial Statements (continued)****12. Income Taxes (continued)**

The components of the deferred tax assets are as follows:

	AS OF DECEMBER 31,	
	2011	2012
Deferred tax assets:		
Net operating loss carryforwards	\$ 15,015	\$ 19,849
Capitalized research and development costs	1,777	1,630
Research and development credit carryforwards	1,333	1,210
Depreciation and other costs	498	166
Deferred tax assets	18,623	22,855
Valuation allowance	(18,623)	(22,855)
Deferred tax assets	\$	\$

Management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its net deferred tax assets and determined that it is more likely than not that the Company will not recognize the benefits of the net deferred tax assets. As a result, a valuation allowance was established at December 31, 2011 and 2012. The valuation allowance increased in 2012 by \$4,232, primarily due to the increase in the Company's net operating loss carryforwards. As of December 31, 2012, the Company has approximately \$47,313 of federal and \$47,028 of state net operating loss carryforwards, and \$664 of federal and \$546 of Massachusetts research and development credits that expire starting in 2028.

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

As of December 31, 2012, the Company had \$563 of unrecognized tax benefits, of which \$563 would affect income tax expense if recognized, before consideration of the valuation allowance. The Company does not expect the unrecognized tax benefits to change significantly over the next 12 months. The Company recognizes both interest and penalties associated with uncertain tax positions as a component of income tax expense. As of December 31, 2012, the Company has not accrued any penalties or made provisions for interest.

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

	AS OF DECEMBER 31,	
	2012	
Unrecognized tax benefits at the beginning of the year	\$	
Additions for current tax positions		563
Lapse of statute of limitations		
Unrecognized tax benefits at the end of the year	\$	563

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Table of Contents**DICERNA PHARMACEUTICALS, INC.****Notes to Financial Statements (continued)****12. Income Taxes (continued)**

The Company files income tax returns in the United States and Commonwealth of Massachusetts. The tax years 2007 through 2012 remain open to examination by these jurisdictions, as carryforward attributes generated in past years may be adjusted in a future period. The Company is not currently under examination by the Internal Revenue Service or any other jurisdiction for these years. The Company has not recorded any interest or penalties for unrecognized tax benefits since its inception.

13. Commitments and Contingencies***Facility lease***

The Company began leasing office and lab space in 2008 under a noncancelable operating lease that, as amended on July 3, 2013, expires on November 30, 2016. The lease agreement provides for an increasing monthly payment over the lease term. Rent expense is recorded on the straight-line basis and, therefore, the Company had a deferred rent obligation in the amount of \$101, \$63 and \$14 as of December 31, 2011 and 2012, and September 30, 2013 (unaudited), respectively. The Company is also required to maintain a letter of credit of \$264 related to the operating lease, which is secured by a certificate of deposit. The certificate of deposit is shown as restricted cash on the accompanying balance sheets.

Rent expense was \$899 for each of the years ended December 31, 2011 and 2012, and was \$674 for each of the nine months ended September 30, 2012 (unaudited) and 2013 (unaudited).

As of December 31, 2012, future minimum payments payable under the facility lease are approximately \$887 for the lease term ending November 30, 2013. Under the amended facility lease terms, future minimum payments payable are approximately as follows:

YEAR ENDING DECEMBER 31	OPERATING LEASES
2013	\$ 936
2014	579
2015	609
2016	584
Total	\$ 2,708

Contract research agreement

In February 2008 (as amended in March 2010), the Company entered into a contract research agreement with an independent corporation (the Corporation) to provide laboratory services, materials, and associated research support for the conduct of a research program related to the

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Company's drug discovery and development programs. Under the terms of the agreement, the Company agreed to pay a minimum of \$600 per year through March 2010 and \$765 per year thereafter through March 2013 for work to be performed in accordance with agreed-upon work plans. The Company recorded research and development expense of \$839 and \$825 in 2011 and 2012, respectively, related to the agreement with the Corporation. In addition, as of December 31, 2011 and 2012, respectively, the Company has prepaid \$148 and \$137 for services to be provided in the following year, which are included in prepaid expenses and other current assets on the accompanying balance sheets. The Company has the right to renew the agreement and may terminate the agreement at the conclusion of any work plan commencing after October 1, 2008, but may be required to pay certain fees incurred by the Corporation up to the date of termination.

City of Hope license agreement

In September 2007, the Company entered into a license agreement with City of Hope, an independent academic research and medical center (the Medical Center). In consideration for the right to develop, manufacture, and

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DICERNA PHARMACEUTICALS, INC.

Notes to Financial Statements (continued)

13. Commitments and Contingencies (continued)

commercialize products based on certain of the Medical Center's intellectual property, the Company paid a one-time, non-refundable license fee and issued shares of the Company's \$0.0001 par value common stock as consideration for the license.

The Company is required to pay an annual license maintenance fee, reimburse the Medical Center for patent costs incurred, and an amount within the range of \$5,000 to \$10,000 upon the achievement of certain milestones, and royalties on future sales, if any. Sublicense and other fees have been accrued and are included in accounts payable as of December 31, 2011 and 2012, respectively. The license agreement will remain in effect until the expiration of the last patents or copyrights licensed under the agreement or until all obligations under the agreement with respect to payment of milestones have terminated or expired. The Company may terminate the license agreement at any time upon 90 days written notice to the Medical Center. The Company recorded research and development expense, related to the agreement with the Medical Center, of \$1,400 and \$1,500 in 2011 and 2012, respectively. Such research and development expense was \$38 for each of the nine months ended September 30, 2012 (unaudited) and 2013 (unaudited).

Plant Bioscience Limited license agreement

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

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

14. Employee Benefit Plan

In January 2008, the Company established a 401(k) retirement plan in which substantially all employees are eligible to participate. Eligible employees may elect to contribute up to the maximum limits, as set by the Internal Revenue Service, of their eligible compensation. The Company made discretionary plan contributions of \$136, \$127, \$105 and \$88 in 2011 and 2012 and for the nine months ended September 30, 2012 (unaudited) and 2013 (unaudited), respectively.

15. Subsequent Event

The Company has evaluated subsequent events which may require adjustment to or disclosure in the financial statements through November 8, 2013, the date on which the December 31, 2012 financial statements were originally issued. For the nine months ended September 30, 2013, the Company evaluated subsequent events through December 31, 2013, the date on which the interim financial statements were originally issued.

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6,000,000 Shares

Dicerna Pharmaceuticals, Inc.

Common Stock

PROSPECTUS

Joint Book-Running Managers

Jefferies

Leerink Partners

Stifel

Co-Lead Manager

Baird

January 29, 2014

