Dicerna Pharmaceuticals Inc
Form 424B5
September 10, 2018
Table of Contents

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-224989

PROSPECTUS SUPPLEMENT

(To prospectus dated May 31, 2018)

7,680,492 Shares

Dicerna Pharmaceuticals, Inc.

Common Stock

$13.02 per share

We are selling 7,680,492 shares of our common stock.

We have granted the underwriters an option to purchase up to 1,152,073 additional shares of common stock.

Our common stock is listed on The Nasdaq Global Select Market under the symbol DRNA. The last reported sale price of our common stock on The Nasdaq Global Select Market on September 6, 2018 was $13.02 per share.

Investing in our common stock involves risks. See Risk Factors beginning on page S-11.

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

	Per Share	Total
Public Offering Price	$ 13.02	$ 100,000,005.84
Underwriting Discounts and Commissions(1)	$ 0.7812	$ 6,000,000.35
Proceeds to Dicerna (before expenses)	$ 12.2388	$ 94,000,005.49

(1) The underwriters will also be reimbursed for certain expenses incurred in this offering. See Underwriting for details.

The underwriters expect to deliver the shares to purchasers on or about September 11, 2018 through the book-entry facilities of The Depository Trust Company.

Joint Book-Running Managers

Citigroup **Leerink Partners** **Stifel**

Lead Co-Managers

H.C. Wainwright & Co. **SunTrust Robinson Humphrey**

September 6, 2018

Table of Contents

We are responsible for the information contained in or incorporated by reference in this prospectus supplement and the accompanying prospectus and in any free-writing prospectus we prepare or authorize. We have not authorized anyone to provide you with different information, and we take no responsibility for any other information others may give you. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in or incorporated by reference into this prospectus supplement or the accompanying prospectus is accurate as of any date other than its date.

TABLE OF CONTENTS

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

In this prospectus supplement, the terms Dicerna, Company, we, us, our and similar terms refer to Dicerna Pharmaceuticals, Inc., a Delaware corporation, and its subsidiaries unless the context otherwise requires.

Each of this prospectus supplement and the accompanying base prospectus is part of a shelf registration statement on Form S-3 that we filed with the Securities and Exchange Commission (SEC).

We provide information to you about this offering of shares of our common stock in two separate documents that are bound together: (1) this prospectus supplement, which describes the specific details regarding this offering and also adds to and updates information contained in the accompanying base prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying base prospectus; and (2) the accompanying base prospectus, including the documents incorporated by reference therein, which provides general information, some of which may not apply to this offering. Generally, when we refer to this prospectus, we are referring to both documents combined. If information in this prospectus supplement is inconsistent with the accompanying base prospectus, you should rely on this prospectus supplement. However, if any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in this prospectus the statement in the document having the later date modifies or supersedes the earlier statement as our business, financial condition, results of operations and prospects may have changed since the earlier dates.

You should rely only on the information contained in, or incorporated by reference into, this prospectus and in any free writing prospectus that we may authorize for use in connection with this offering. We have not, and the underwriters have not, authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriters are not making an offer to sell or soliciting an offer to buy our securities in any jurisdiction in which an offer or solicitation is not authorized or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should assume that the information appearing in this prospectus, the documents incorporated by reference into this prospectus, and in any free writing prospectus that we may authorize for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus, the documents incorporated by reference into this prospectus, and any free writing prospectus that we may authorize for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus entitled Where You Can Find More Information and Incorporation of Certain Documents by Reference.

Other than in the U.S., no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. We are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons outside the U.S. who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus outside the U.S. This prospectus does not constitute, and may not be used in connection with, an offer to sell, or a solicitation

Table of Contents

of an offer to buy, any securities offered by this prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

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.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been or will be filed as exhibits to the registration statement of which this prospectus is a part or as exhibits to documents incorporated by reference herein, and you may obtain copies of those documents as described below under the headings Where You Can Find More Information and Incorporation of Certain Documents by Reference.

Table of Contents

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in the securities covered by this prospectus. For a more complete understanding of Dicerna and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus, including the information incorporated by reference in this prospectus and the information included in any free writing prospectus that we have authorized for use in connection with this offering, including the information referred to under the heading Risk Factors in this prospectus supplement beginning on page S-11 and in the other periodic reports incorporated by reference herein.

Overview

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

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

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

Development Programs

In choosing which development programs to advance, we apply scientific, clinical, and commercial criteria that we believe allow us to best leverage our GalXC RNAi platform and maximize value. The Company is focusing its efforts on three priority therapeutic programs that currently have a Clinical Trial Application (CTA) filed, Investigational New Drug application (IND) filed, or are in enabling studies in preparation to

Table of Contents

submit additional regulatory applications that will be necessary to initiate clinical trials. The Company is also focusing its efforts on a series of programs in the clinical candidate selection stage that may be elevated into IND/CTA enabling studies in the future, either on our own or in collaboration with larger pharmaceutical companies. Our three priority programs are: DCR-PHXC for the treatment of primary hyperoxaluria (PH); a program for an undisclosed rare disease; and DCR-HBVS for the treatment of chronic hepatitis B virus (HBV) infection. Our programs in clinical candidate selection include a program for the treatment of hypercholesterolemia, for which DCR-PCSK9 has been selected as a provisional clinical candidate, and multiple programs targeting undisclosed targets in chronic liver diseases, cardiovascular diseases and additional rare diseases. In October 2017, we filed a CTA for our lead GalXC product candidate, DCR-PHXC, with the Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom (UK), and in December 2017, we dosed the first human in the Group A portion of the Phase 1 clinical trial of DCR-PHXC. On March 30, 2018, we received a notice from the United States (U.S.) Food and Drug Administration (FDA) indicating that our proposed clinical investigation for DCR-PHXC referenced in our IND may proceed. In May 2018, the Company dosed the first PH patient with DCR-PHXC in the Group B portion of the Phase 1 clinical trial and received notice from the FDA granting Orphan Drug Designation to DCR-PHXC for treatment of PH. In July 2018, the European Medicines Agency (EMA) s Committee for Orphan Medicinal Products (COMP) recommended designating DCR-PHXC as an orphan medicinal product for the treatment of PH in the European Union (EU) and the recommendation was adopted by the European Commission in August 2018. We have received regulatory and ethical approvals for the clinical trial in the UK, France, and Germany. A CTA has been submitted and is pending approval in the Netherlands. We expect to submit requests for additional regulatory clearances necessary to commence clinical trials for our programs in 2018 and 2019.

The table below sets forth the state of development of our various GalXC RNAi platform product candidates as of August 8, 2018.

Table of Contents

Our current GalXC RNAi platform development programs are as follows:

Primary Hyperoxaluria. We are developing DCR-PHXC for the treatment of all types of PH. PH is a family of rare inborn errors of metabolism in which the liver produces excessive levels of oxalate, which in turn causes damage to the kidneys and other tissues in the body. DCR-PHXC is currently being investigated in a Phase 1 clinical trial called PHYOX. In nonclinical models of PH, DCR-PHXC reduces oxalate production to near-normal levels, ameliorating the disease condition.

PHYOX is a Phase 1 single ascending-dose study of DCR-PHXC in normal healthy volunteers (NHVs) and patients with PH. The study is divided into two groups: Group A is a placebo-controlled, single-blind, single center study, which has enrolled 25 NHVs; Group B is an open-label, multi-center study enrolling up to 16 patients with PH type 1 (PH1) and PH type 2 (PH2). The primary objective of the trials is to evaluate the safety and tolerability of single doses of DCR-PHXC in both groups. The secondary objectives are to evaluate the pharmacodynamic effect of single doses of DCR-PHXC on biochemical markers, and to characterize the pharmacokinetics of single doses of DCR-PHXC in NHVs and patients with PH. We have submitted CTAs for the PHYOX trial in the UK, France, and Germany and have received the required regulatory and ethical approvals. A CTA has been submitted and is pending approval in the Netherlands. The FDA has accepted the Company s IND for the PHYOX trial. We have completed the Group A portion of the study in NHVs. While the study is still blinded toward treatment assignment, there have been no serious adverse events. There have been two mild-to-moderate transient injection site reactions lasting up to a total of 36 hours at the highest doses of 6 and 12 mg/kg. With the completion of the Group A portion of the study in NHVs, we have started on the Group B portion of the study and dosed the first PH patient with DCR-PHXC. Group B consists of three cohorts of patients with PH1 dosed at 1.5, 3, and 6 mg/kg. An additional fourth cohort consists of patients with PH2 dosed at a flexible dosing level. We have enrolled 10 patients out of 16 (four PH1 patients in Cohort 1, four PH1 patients in Cohort 2, one PH1 patient in Cohort 3, and one PH2 patient in Cohort 4). We reported interim results from the PHYOX trial on September 5, 2018 and expect to publicly present trial results in the fourth quarter of 2018. See Recent Developments. Additionally, we intend to initiate a multi-dose registration trial in the first quarter of 2019, pending regulatory feedback, with data readout expected in 2020.

An undisclosed rare disease involving the liver. We are developing a GalXC-based therapeutic, targeting a liver-expressed gene involved in a serious rare disease. For competitive reasons, we have not yet publicly disclosed the target gene or disease. We have selected this target gene and disease based on criteria that include having a strong therapeutic hypothesis, a readily-identifiable patient population, the availability of a potentially predictive biomarker, high unmet medical need, favorable competitive positioning and what we believe is a rapid projected path to approval. The disease is a genetic disorder where mutations in the disease gene lead to the production of an abnormal protein. The protein causes progressive liver damage and fibrosis, in some cases leading to cirrhosis and liver failure, and we believe that silencing of the disease gene will prevent production of the abnormal protein and thereby slow or stop progression of the liver fibrosis. Greater than 100,000 people in the U.S. are believed to be homozygous (i.e. having identical pairs of genes for any given pair of hereditary characteristics) for the mutation that causes the liver disease, and at least 10% of those people, and potentially a significantly higher fraction, are believed to have liver-associated disease as a consequence. We are seeking a risk-sharing collaborator for this program before we submit requests for regulatory clearances to initiate clinical trials, which we expect to be prepared to file towards the end of 2018.

Chronic Hepatitis B Virus infection. We have declared a GalXC RNAi platform-based product candidate for the treatment of HBV, DCR-HBVS, and are conducting formal non-clinical development studies. We expect to file regulatory clearances in New Zealand and Australia during the fourth quarter of 2018. Current therapies for HBV rarely lead to a long-term immunological cure as measured by the clearance of HBV surface antigen (HBsAg) and sustained HBV deoxyribonucleic acid (DNA) suppression in patient plasma or blood. DCR-HBVS targets HBV messenger RNA and leads to greater

Table of Contents

than 99% reduction in circulated HBsAg in mouse models of HBV infection. Based on these preclinical studies, and only if we receive appropriate regulatory approval to begin human clinical trials, we hope to determine the potential of DCR-HBVS to reduce HBsAg and HBV DNA levels in the blood of HBV patients in a commercially attractive subcutaneous dosing paradigm.

Hypercholesterolemia (PCSK9 targeted therapy). We are using our GalXC RNAi platform to develop a therapeutic that targets the PCSK9 gene for the treatment of hypercholesterolemia. The Company has selected a provisional clinical candidate for the program but is continuing to explore ways to further optimize the program. PCSK9 is a validated target for hypercholesterolemia, and there are FDA-approved therapies targeting PCSK9 that are based on monoclonal antibody technology. Based on preclinical studies, we believe that our GalXC RNAi platform has the potential to produce a PCSK9-targeted therapy with attractive commercial properties, such as small subcutaneous injection volumes and less frequent dosing.

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

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

Table of Contents

included in the preclinical studies up to an agreed-upon limit. We are eligible to receive up to $191.0 million in potential development and commercial milestones related to the initial target. We are also eligible to receive royalty payments on potential global net sales, subject to certain adjustments, tiered from high single digits up to low double digits. BI s option to add a second target would provide for an option fee payment and success-based development and commercialization milestones and royalty payments to us. We also have developed a wholly-owned clinical candidate, DCR-BCAT, targeting the ß-catenin oncogene. DCR-BCAT is based on an extended version of our earlier generation non-GalXC Dicer Substrate RNAi technology and is delivered by our lipid nanoparticle tumor delivery system, EnCore™. We plan to out-license, spin out or seek external funding to advance the DCR-BCAT opportunity, given our focus on our GalXC platform-based programs.

Corporate Developments

On April 18, 2018, we entered into a Confidential Settlement Agreement and General Release (the Settlement Agreement) with Alnylam Pharmaceuticals, Inc. (Alnylam), resolving all ongoing litigation between the Company and Alnylam. The terms of the Settlement Agreement include mutual releases and dismissals with prejudice of all claims and counterclaims in the following litigation between the parties: (i) *Alnylam Pharmaceuticals, Inc. v. Dicerna Pharmaceuticals, Inc.*, No. 15-4126 pending in the Massachusetts Superior Court for Middlesex County and (ii) *Dicerna Pharmaceuticals, Inc., v. Alnylam Pharmaceuticals, Inc.* No.1:17-cv-11466 pending in the United States District Court for the District of Massachusetts. Pursuant to the terms of the Settlement Agreement, we have agreed to make the following payments to Alnylam: (i) a $2.0 million upfront payment in cash, which we made in May 2018; (ii) an additional $13.0 million in cash, to be paid as 10% of any upfront or first year cash consideration that we receive pursuant to future collaborations related to Ga1NAc-conjugated RNAi research and development (excluding any amounts received or to be received by the Company from its existing collaboration with BI), provided that the $13.0 million must be paid by no later than April 28, 2022; and (iii) issuance of shares of our common stock (the Shares) pursuant to a share issuance agreement between the parties (the Share Issuance Agreement).

Under the Settlement Agreement, for periods ranging from 18 months up to four years, we will be restricted in our development and other activities relating to oligonucleotide-based therapeutics directed toward a defined set of eight Alnylam targets (the Oligo Restrictions). The Oligo Restrictions pertain to targets where Dicerna does not have, or does not currently intend to have, a therapeutic program, or are expected to be consistent with our execution on programs in the normal course of business. The Settlement Agreement does not include any admission of liability or wrongdoing by either party or any licenses to any other intellectual property from either party.

On April 20, 2018, we entered into the Share Issuance Agreement, pursuant to which we agreed to issue to Alnylam 983,208 Shares in satisfaction of our obligation under the Settlement Agreement to deliver Shares to Alnylam. The Share Issuance Agreement contains customary representations and warranties of each party. Pursuant to the terms of the Share Issuance Agreement, Alnylam may not, without our prior approval, dispose of any of the Shares for a six-month period commencing on the closing date of the Share issuance. Thereafter, through the fifth anniversary of the closing date of the Share issuance, Alnylam will only dispose of the maximum number of Shares that it would be permitted to dispose if the Shares were subject to the volume restrictions set forth in Rule 144(e) of the Securities Act of 1933, as amended.

Risk Factors

Our business is subject to numerous risks, which are highlighted in and incorporated in the section entitled Risk Factors in this prospectus.

Table of Contents

Our Corporate Information

We were incorporated in Delaware in October 2006. Our mailing address is 87 Cambridgepark Drive, Cambridge, MA 02140 where our principal executive offices are located, and our main telephone number is (617) 621-8097. We maintain a website at 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.

Table of Contents

RECENT DEVELOPMENTS

We announced on September 5, 2018 preliminary proof-of-concept data from its ongoing PHYOX Phase 1 clinical trial. A single-dose administration of DCR-PHXC, the Company s lead GalXC product candidate, brought urinary oxalate levels into the normal range (defined as 24-hour excretion £0.46 mmol) or near-normal range (defined as 24-hour excretion £0.6 mmol) in a majority of the eight assessed patients with primary hyperoxaluria type 1 and type 2 (PH1 and PH2). All of the assessed patients experienced substantial and clinically significant reductions in urinary oxalate (defined as >30% reduction compared to baseline). Assessed patients are those patients for whom data are available through Week 6, or Day 43. All assessed patients are adults and include seven patients with PH1 and one patient with PH2.

The interim PHYOX data constitute preliminary clinical proof of concept for DCR-PHXC. Moreover, the investigational agent was safe and well-tolerated during the period of initial observation. The interim data provide a promising indicator of DCR-PHXC s potential potency and duration of action following administration of a single dose, and are consistent with an anticipated once-quarterly administration. Dicerna intends to present a detailed data readout from the PHYOX trial in the fourth quarter of 2018, and plans to initiate a registration trial for DCR-PHXC, pending regulatory feedback, in the first quarter of 2019, with data readout expected in 2020.

The Company is investigating DCR-PHXC for the treatment of all forms of PH, a family of severe, rare, inherited disorders of the liver that often result in kidney failure. The Company initiated the PHYOX trial in NHVs in the fourth quarter of 2017 and dosed the first patient with PH in May 2018.

The primary objective of the PHYOX trial (ClinicalTrials.gov: NCT03392896) is to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of single-ascending doses of DCR-PHXC. Secondary endpoints include the change in 24-hour urinary oxalate excretion from baseline, defined as the mean of two 24-hour collections during screening. The trial is divided into two groups:

Group A is a placebo-controlled, single-blind Phase 1 trial in 25 NHVs enrolled at a single site in the United Kingdom.

Group B is an open-label, multi-center trial of DCR-PHXC in 16 patients with PH, including three cohorts of patients with PH1 dosed at 1.5, 3.0, and 6.0 mg/kg, and a fourth PH2-only cohort with flexible dosing. Group B patients are being enrolled at five sites in the EU and one site in the United States.

Initial Results in PHYOX Phase 1 Trial Group B

In the first Group B cohort (1.5 mg/kg), preliminary results following a single administration of DCR-PHXC show that three of four adult patients had urinary oxalate levels in the near-normal range between Days 43 and 57, which are the latest observation days for those patients. The fourth adult, whose baseline urinary oxalate level was 2.28 mmol/24hr, is exhibiting substantial reductions, with the latest observation (Day 95) showing the maximal reduction for that patient (urinary oxalate <1.0 mmol/24hr).

In the second Group B cohort (3 mg/kg), two of four adult patients reached normal urinary oxalate concentrations (<0.46 mmol/24hr) by Day 43. Both of the other patients also have substantial oxalate reductions (one of which does not yet have Day 43 data). The one adult patient with PH2 in the fourth Group B cohort has also experienced a substantial reduction in 24-hour urinary oxalate excretion. The PHYOX investigators have observed three mild-to-moderate injection site reactions. All were transient and resolved without intervention.

Table of Contents

THE OFFERING

Common stock offered by us	7,680,492 shares
Underwriters option to purchase additional shares	We have granted the underwriters an option to purchase up to 1,152,073 additional shares of our common stock. This option is exercisable, in whole or in part, for a period of 30 days from the date of this prospectus supplement.
Common stock to be outstanding immediately after this offering	60,654,832 shares (as more fully described in the notes following this table) (61,806,905 shares if the underwriters exercise their option to purchase additional shares in full).
Use of Proceeds	

We currently intend to use the net proceeds from this offering for preclinical studies and clinical trials, and to use the remainder of any net proceeds for continued technology platform development, working capital and general corporate purposes. See Use of Proceeds.

Risk Factors

Investing in our securities involves a high degree of risk. See Risk Factors beginning on page S-11 of this prospectus supplement and the other information included in, or incorporated by reference into, this prospectus for a discussion of certain factors that you should carefully consider before deciding to invest in shares of our common stock.

Nasdaq Global Select Market Symbol

Our common stock is listed on The Nasdaq Global Select Market under the symbol DRNA.

The number of shares of our common stock shown above to be outstanding immediately after this offering is based on 52,974,340 shares outstanding as of September 4, 2018 and excludes:

- 2,198 shares of our common stock issuable upon the exercise of outstanding warrants as of September 4, 2018, at a weighted average exercise price of $250.00 per share;
- 7,625,999 shares of our common stock issuable upon the exercise of outstanding options as of September 4, 2018, at a weighted average exercise price of $9.07 per share; and

1,364,246 shares of our common stock available for future issuance pursuant to our existing stock incentive plans as of September 4, 2018.

Table of Contents

RISK FACTORS

We face a variety of significant and diverse risks, many of which are inherent in our business. You should carefully consider the risks described under the caption Risk Factors in our most recent annual report on Form 10-K, subsequent quarterly reports on Form 10-Q and other filings we make with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended (the Exchange Act), incorporated by reference herein, before making an investment decision. In addition to such other risks, set forth below are risks related to this offering. The occurrence of any of the risks set forth above or below could materially and adversely affect our business, prospects, financial condition, results of operations or cash flow. Other risks and uncertainties that we do not now consider to be material or of which we are not now aware may become important factors that affect us in the future. You should carefully consider the risks and uncertainties described below and in the documents incorporated by reference herein before deciding to invest in our common stock.

Additional Risks Related to This Offering

We have broad discretion in the use of the net proceeds from this offering.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways with which you may not agree. Accordingly, you will be relying on the judgment of our management with regard to the use of the 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 net proceeds will be invested or otherwise used in a way that does not yield a favorable, or any, return for the Company.

Investors in this offering will experience immediate and substantial dilution in the net tangible book value per share of the common stock they purchase.

Since the price per share of our common stock being offered is higher than the net tangible book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. See the section entitled Dilution in this prospectus for a more detailed discussion of the dilution you will incur immediately after this offering if you purchase common stock in this offering. In addition, we have a significant number of options and a number of warrants outstanding. If the holders of these options or warrants exercise such options or warrants, you may incur further dilution.

Our stockholders may experience significant dilution as a result of future equity offerings and exercise of outstanding options.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock, as we did with the Redeemable Convertible Preferred (as defined below), which was converted into common stock in December 2017. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share in this offering.

In addition, we have a significant number of securities allowing the purchase of our common stock. As of September 4, 2018, we also had 1,364,246 shares of common stock reserved for future issuance under our stock incentive plans. As of that date, there were also stock options and awards to purchase 7,625,999 shares of our common stock outstanding and warrants to purchase 2,198 shares of our common stock outstanding. The exercise of outstanding options and warrants having an exercise price per share that is less than the offering price per share in this offering will increase dilution to investors in this offering.

Table of Contents

Future sales of our common stock in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. As of September 4, 2018, we had 52,974,340 shares of common stock outstanding, all of which shares, other than shares held by our directors and certain officers, were eligible for sale in the public market, subject in some cases to compliance with the requirements of Rule 144, including the volume limitations and manner of sale requirements. In addition, shares of common stock issuable upon exercise of outstanding options and warrants and shares reserved for future issuance under our stock incentive plans will become eligible for sale in the public market to the extent permitted by applicable vesting requirements and subject in some cases to compliance with the requirements of Rule 144.

Risks Related to Our Business

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

We will need to raise substantial additional funds to expand our development, regulatory, manufacturing, marketing, and sales capabilities, whether internally or through other organizations. We have used substantial funds to develop our product candidates and delivery technologies and will require significant funds to conduct further research and development and preclinical testing and clinical trials of our product candidates, to seek regulatory approvals for our product candidates, and to manufacture and market products, if any are approved for commercial sale. As of June 30, 2018, we had $82.3 million in cash and cash equivalents and held-to-maturity investments. Based on our current operating plan and liquidity, we believe that our available cash, cash equivalents, and held-to-maturity investments will be sufficient to fund our planned level of operations for at least the 12-month period following September 4, 2018. Our future capital requirements and the period for which we expect our existing resources to support our operations may vary significantly from what we expect. Our monthly spending levels vary based on new and ongoing development and corporate activities. Because the length of time and activities associated with successful development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. To execute our business plan, we will need, among other things:

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

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

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

If we are unable to obtain funding on a timely basis or on acceptable terms, we may have to delay, reduce, or terminate our research and development programs and preclinical studies or clinical trials, if any, limit strategic opportunities, or undergo reductions in our workforce or other corporate restructuring activities. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies or product candidates that we would otherwise pursue on our own.

Table of Contents

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

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

We are a biopharmaceutical company with a limited operating history focused on the discovery and development of treatments based on the emerging therapeutic modality RNAi, a biological process in which RNA molecules inhibit gene expression. Since our inception in October 2006, we have devoted our resources to the development of DsiRNA molecules and delivery technologies. We have had significant operating losses since our inception. As of June 30, 2018, we had an accumulated deficit of $367.2 million. For the six months ended June 30, 2018 and for the years ended December 31, 2017, 2016, and 2015, our net loss attributable to common stockholders was $51.2 million, $80.1 million, $59.5 million, and $62.8 million, respectively. Substantially all of our operating losses have resulted from expenses incurred in connection with our research and development programs, general and administrative costs associated with our operations and litigation expenses associated with the Alnylam litigation settled in April 2018. Our technologies and product candidates are in early stages of development, and we are subject to the risks of failure inherent in the development of product candidates based on novel technologies.

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

Table of Contents

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

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

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

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

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

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

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

Table of Contents

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

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

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