UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

Form 10-Q

☑ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended June 30, 2021

OR

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

For the transition period from _____ to _____

Commission File Number: 001-36281

DICERNA PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**20-5993609**
(State or other jurisdiction of incorporation or organization)	**(IRS Employer Identification No.)**
75 Hayden Avenue Lexington, MA	**02421**
(Address of principal executive offices)	**(Zip code)**

(617) 621-8097

(Registrant's telephone number, including area code)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 Par Value	DRNA	The Nasdaq Global Select Market

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☑ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer,"

“smaller reporting company,” and “emerging growth company” in Rule 12b-2 of the Exchange Act:

Large accelerated filer	☑	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☐

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

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

As of August 2, 2021, there were 77,734,172 shares of the registrant’s common stock, par value $0.0001 per share, outstanding.

DICERNA PHARMACEUTICALS, INC.
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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

- future conduct of the business of the Company, its preclinical studies, clinical programs, and operations, including in relation to the COVID-19 pandemic;
- the research and development plans and timelines related to the Company's clinical programs, including the opportunity to enroll, continue, or resume clinical studies that are slowed or halted by the COVID-19 pandemic;
- the initiation, timing, progress, and results of our preclinical studies and Investigational New Drug Applications, Clinical Trial Applications, New Drug Applications, and other regulatory submissions;
- our alignment with the United States ("U.S.") Food and Drug Administration on regulatory approval requirements;
- identification and development of product candidates for the treatment of additional disease indications;
- obtaining and maintaining regulatory approval of any of our product candidates;
- the rate and degree of market acceptance of any approved product candidates;
- our strategy for, and the commercialization of any approved product candidates;
- our ability to maintain existing and establish additional collaborations and retain commercial rights with respect to some or all of our product candidates in the collaborations;
- the execution of our business model and strategic plans for our business, technologies, and product candidates;
- how long we expect to maintain liquidity to fund our planned level of operations and our ability to obtain additional funds for our operations and growth;
- our estimates of our expenses, ongoing losses, future revenue, and capital requirements;
- obtaining, maintaining, and defending intellectual property protection for our technologies and product candidates and our freedom to operate our business without infringing the intellectual property rights of others;
- our reliance on third parties to conduct our preclinical development studies or any clinical trials;
- the continued manufacture and supply of raw materials and components for the Company's clinical and development programs, the availability of any of which could be significantly impaired by the COVID-19 pandemic;
- our ability to attract and retain qualified key management and personnel;
- our dependence on our existing collaborators, Novo Nordisk A/S, Roche, Eli Lilly and Company, Alexion Pharmaceuticals, Inc., Boehringer Ingelheim International GmbH, and Alnylam Pharmaceuticals, Inc. for developing, obtaining regulatory approval for, and commercializing product candidates in the collaborations;
- our receipt and timing of any potential milestone payments or royalties under our existing research collaborations and license agreements or any future arrangements with our existing collaboration partners or any other collaborators;
- the impact of changes in the government and agency leadership positions in connection with the 2020 presidential election as well as future election cycles;
- our financial performance; and
- developments relating to our competitors or our industry.

These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties, and other factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those set forth in Part II, Item 1A – "Risk Factors" below and for the reasons described elsewhere in this Quarterly Report on Form 10-Q. Any forward-looking statement in this Quarterly Report on Form 10-Q reflects our current view with respect to future events and is subject to these and other risks, uncertainties, and assumptions relating to our operations, results of operations, industry, and future growth. Given these uncertainties,

you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

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

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

Trademarks

This Quarterly Report on Form 10-Q includes trademarks, service marks, and trade names owned by us or other companies. All trademarks, service marks, and trade names included in this Quarterly Report on Form 10-Q are the property of their respective owners. Solely for convenience, the trademarks, service marks, and trade names in this report may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Risk Factor Summary

Our business is subject to numerous risks and uncertainties. These risks represent challenges to the successful implementation of our strategy and to the growth and future profitability of our business. These risks include, but are not limited to, the following:

- Business interruptions resulting from the coronavirus disease (COVID-19) outbreak or similar public health crises could cause a disruption to the development of our product candidates and adversely impact 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. Raising additional funds may cause dilution to our stockholders, restrict our operations, or require us to relinquish control over our technologies or product candidates.
- Our approach to the discovery and development of innovative therapeutic treatments based on novel technologies is unproven and may not result in marketable products.
- 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.
- Our product candidates are in varied stages of development, including some in early stages, and may fail or suffer delays that materially and adversely affect their commercial viability.
- Breakthrough Therapy Designation by the FDA may not actually lead to a faster development or regulatory review or approval process.
- The approval of our planned marketing application for nedosiran may be delayed due to the failure to satisfy FDA regulatory requirements, resulting in changes to or a delay in the commercial launch of nedosiran.
- We are dependent on our collaboration partners for the successful development of some product candidates and, therefore, are subject to the efforts of these partners and our ability to successfully collaborate with these partners.
- Because we rely on third-party manufacturing and supply partners, our supply of research and development, preclinical studies, and clinical trial materials may become limited or interrupted or may not be of satisfactory quantity or quality, and if the third parties on which we depend do not perform as contractually required, our development programs could be delayed with materially adverse effects on our business, financial condition, results of operations, and prospects.
- Interim and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available or as additional analyses are conducted and as the data are subject to audit and verification procedures that could result in material changes in the final data.
- We may be unable to successfully commercialize our product candidates if 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, if at all.

- We may be unable to successfully commercialize product candidates if the regulatory-approved labeling for our product candidates does not enable us to appropriately differentiate our products from competitive products.
- Price controls imposed in foreign markets and downward pricing pressure in the U.S. may adversely affect our future profitability.
- Our current operations are largely concentrated in one location and any events affecting this location may have material adverse consequences.
- We may be unable to protect our intellectual property rights throughout the world.
- We may be unable to obtain U.S. or foreign regulatory approval and, as a result, may be unable to commercialize our product candidates.
- Our ability to obtain reimbursement or funding from the federal government may be impacted by possible reductions in federal spending and our ability to maintain such reimbursement or funding may be impacted due to our failure to satisfy federal requirements with respect thereto.
- Recent federal legislation and actions by state and local governments may permit reimportation of drugs from foreign countries into the U.S., including foreign countries where the drugs are sold at lower prices than in the U.S., which could materially adversely affect our operating results.
- 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.
- Any inability to attract and retain qualified key management and personnel would impair our ability to implement our business plan.

PART I. FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

DICERNA PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(Unaudited)
(in thousands, except share data)

	JUNE 30, 2021	DECEMBER 31, 2020
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 221,210	$ 126,023
Held-to-maturity investments, current	371,755	442,820
Restricted cash equivalents, current	—	744
Contract receivables	3,147	34,713
Prepaid expenses and other current assets	20,380	14,403
Total current assets	616,492	618,703
NONCURRENT ASSETS:		
Property and equipment, net	23,593	17,546
Right-of-use operating assets, net	74,400	60,843
Restricted cash equivalents, noncurrent	5,618	5,618
Held-to-maturity investments, noncurrent	116,599	—
Other noncurrent assets	1,790	5,136
Total noncurrent assets	222,000	89,143
TOTAL ASSETS	$ 838,492	$ 707,846
LIABILITIES AND STOCKHOLDERS' EQUITY		
CURRENT LIABILITIES:		
Accounts payable	$ 12,829	$ 7,901
Accrued expenses and other current liabilities	29,577	28,061
Lease liability, current	3,946	3,439
Deferred revenue, current	160,200	138,537
Deferred income, current	1,098	—
Total current liabilities	207,650	177,938
NONCURRENT LIABILITIES:		
Lease liability, noncurrent	61,203	48,744
Deferred revenue, noncurrent	268,606	336,236
Deferred income, noncurrent	178,708	—
Derivative liability	7,750	6,000
Other noncurrent liabilities	3,501	1,174
Total noncurrent liabilities	519,768	392,154
TOTAL LIABILITIES	727,418	570,092
COMMITMENTS AND CONTINGENCIES (NOTE 11)		
STOCKHOLDERS' EQUITY:		
Preferred stock, $0.0001 par value – 5,000,000 shares authorized; no shares issued or outstanding at June 30, 2021 or December 31, 2020	—	—
Common stock, $0.0001 par value – 150,000,000 shares authorized; 77,601,552 and 75,757,213 shares issued and outstanding at June 30, 2021 and December 31, 2020, respectively	8	8
Additional paid-in capital	819,909	775,809
Accumulated deficit	(708,843)	(638,063)
Total stockholders' equity	111,074	137,754
TOTAL LIABILITIES AND STOCKHOLDERS' EQUITY	$ 838,492	$ 707,846

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

DICERNA PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(Unaudited)
(in thousands, except share and per share data)

	THREE MONTHS ENDED JUNE 30,		SIX MONTHS ENDED JUNE 30,	
	2021	2020	2021	2020
Revenue	$ 41,337	$ 40,448	$ 88,940	$ 74,476
Operating expenses:				
Research and development	56,119	53,376	112,157	96,547
General and administrative	25,462	20,565	46,134	36,588
Total operating expenses	81,581	73,941	158,291	133,135
Loss from operations	(40,244)	(33,493)	(69,351)	(58,659)
Other income (expense):				
Interest income	111	1,729	391	4,342
Interest expense	(4)	(6)	(8)	(10)
Other (expense) income	(132)	(50)	(1,266)	15
Total other (expense) income	(25)	1,673	(883)	4,347
Loss before income taxes	(40,269)	(31,820)	(70,234)	(54,312)
Provision for income taxes	(546)	—	(546)	—
Net loss	$ (40,815)	$ (31,820)	$ (70,780)	$ (54,312)
Net loss per share – basic and diluted	$ (0.53)	$ (0.43)	$ (0.92)	$ (0.74)
Weighted average common shares outstanding – basic and diluted	77,029,763	74,001,126	76,644,786	73,460,252

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

DICERNA PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY
(Unaudited)
(in thousands, except share data)

	SIX MONTHS ENDED JUNE 30, 2021				
	COMMON STOCK		ADDITIONAL PAID-IN CAPITAL	ACCUMULATED DEFICIT	TOTAL STOCKHOLDERS' EQUITY
	SHARES	AMOUNT			
BALANCE – January 1, 2021	75,757,213	$ 8	$ 775,809	$ (638,063)	$ 137,754
Exercises of common stock options	707,723	—	7,616	—	7,616
Vesting of restricted stock units	177,950	—	—	—	—
Shares withheld to cover taxes upon restricted stock unit vesting	(59,012)	—	(1,414)	—	(1,414)
Stock-based compensation expense	—	—	12,413	—	12,413
Net loss	—	—	—	(29,965)	(29,965)
BALANCE – March 31, 2021	76,583,874	8	794,424	(668,028)	126,404
Exercises of common stock options and sales of common stock under Employee Stock Purchase Plan	957,564	—	12,314	—	12,314
Vesting of restricted stock units	73,073	—	—	—	—
Shares withheld to cover taxes upon restricted stock unit vesting	(12,959)	—	(462)	—	(462)
Stock-based compensation expense	—	—	13,633	—	13,633
Net loss	—	—	—	(40,815)	(40,815)
BALANCE – June 30, 2021	77,601,552	$ 8	$ 819,909	$ (708,843)	$ 111,074

	SIX MONTHS ENDED JUNE 30, 2020				
	COMMON STOCK		ADDITIONAL PAID-IN CAPITAL	ACCUMULATED DEFICIT	TOTAL STOCKHOLDERS' EQUITY
	SHARES	AMOUNT			
BALANCE – January 1, 2020	71,573,196	$ 7	$ 677,504	$ (525,316)	$ 152,195
Exercises of common stock options	128,373	—	588	—	588
Stock-based compensation expense	—	—	8,527	—	8,527
Proceeds from issuance of common stock, net of commissions and offering costs of $904	2,077,500	—	39,088	—	39,088
Net loss	—	—	—	(22,492)	(22,492)
BALANCE – March 31, 2020	73,779,069	7	725,707	(547,808)	177,906
Exercises of common stock options and sales of common stock under Employee Stock Purchase Plan	542,256	—	5,876	—	5,876
Stock-based compensation expense	—	—	10,206	—	10,206
Net loss	—	—	—	(31,820)	(31,820)
BALANCE – June 30, 2020	74,321,325	$ 7	$ 741,789	$ (579,628)	$ 162,168

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

DICERNA PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(Unaudited)
(in thousands)

	SIX MONTHS ENDED JUNE 30,	
	2021	**2020**
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (70,780)	$ (54,312)
Adjustments to reconcile net loss to net cash provided by operating activities:		
Stock-based compensation expense	26,046	18,733
Change in fair value of derivative liability	1,750	—
Depreciation and amortization expense	2,487	1,066
Accretion (amortization) of premium on investments	1,965	(302)
Non-cash lease expense	5,550	3,640
Other	42	(5)
Changes in operating assets and liabilities:		
Deferred revenue	(45,967)	117,243
Deferred income	179,806	—
Prepaid expenses and other assets	(4,481)	(11,988)
Accounts payable	4,810	2,035
Contract receivables	31,566	200,342
Accrued expenses and other liabilities	3,525	7,536
Lease liability	(4,182)	(4,564)
Net cash provided by operating activities	132,137	279,424
CASH FLOWS FROM INVESTING ACTIVITIES:		
Maturities of held-to-maturity investments	344,000	254,000
Purchases of held-to-maturity investments	(391,498)	(529,041)
Purchases of property and equipment	(8,223)	(3,358)
Other	—	15
Net cash used in investing activities	(55,721)	(278,384)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from issuance of common stock, net of placement agent commissions	—	39,192
Payments of common stock offering costs	—	(104)
Payments for minimum statutory tax withholding related to net share settlement of equity awards	(1,876)	—
Proceeds from exercises of stock options	19,925	6,550
Other	(22)	(24)
Net cash provided by financing activities	18,027	45,614
NET INCREASE IN CASH, CASH EQUIVALENTS, AND RESTRICTED CASH EQUIVALENTS	94,443	46,654
CASH, CASH EQUIVALENTS, AND RESTRICTED CASH EQUIVALENTS – Beginning of period	132,385	156,710
CASH, CASH EQUIVALENTS, AND RESTRICTED CASH EQUIVALENTS – End of period	$ 226,828	$ 203,364

	SIX MONTHS ENDED JUNE 30,	
	2021	2020
SUPPLEMENTAL CASH FLOW INFORMATION:		
NONCASH OPERATING ACTIVITIES		
Right-of-use assets acquired through operating leases	$ 15,302	$ 1,101
NONCASH INVESTING ACTIVITIES		
Property and equipment purchases included in accounts payable and accrued expenses	$ 177	$ 446
NONCASH FINANCING ACTIVITIES		
Right-of-use assets acquired through financing leases	$ —	$ 48

The following table provides a reconciliation of cash, cash equivalents, and restricted cash equivalents reported within the condensed consolidated balance sheets to the amounts shown in the condensed consolidated statements of cash flows:

	SIX MONTHS ENDED JUNE 30,	
	2021	2020
Cash and cash equivalents	$ 221,210	$ 197,801
Restricted cash equivalents, noncurrent	5,618	5,563
Total cash, cash equivalents, and restricted cash equivalents shown in the condensed consolidated statements of cash flows	$ 226,828	$ 203,364

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

DICERNA PHARMACEUTICALS, INC.
NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS
(Unaudited)
(amounts in thousands, except share and per share data and where otherwise noted)

1. DESCRIPTION OF BUSINESS AND BASIS OF PRESENTATION

Business

Dicerna Pharmaceuticals, Inc. (the "Company" or "Dicerna") is a biopharmaceutical company focused on discovering, developing, and commercializing medicines that are designed to leverage ribonucleic acid interference ("RNAi") to silence selectively genes that cause or contribute to disease. Using the Company's proprietary GalXC™ and GalXC-Plus™ RNAi technologies, Dicerna is committed to developing RNAi-based therapies with the potential to treat both rare and more prevalent diseases. By silencing disease-causing genes, Dicerna's GalXC platform has the potential to address conditions that are difficult to treat with other modalities. Initially focused on disease-causing genes in the liver, Dicerna has continued to innovate and is exploring new applications of its RNAi technology with GalXC-Plus, which expands the functionality and application of the Company's flagship liver-based GalXC technology to tissues and cell types outside the liver and has the potential to treat diseases across multiple therapeutic areas. In addition to the Company's own pipeline of core discovery and clinical candidates, Dicerna has established collaborative relationships with some of the world's leading pharmaceutical companies, including Novo Nordisk A/S ("Novo"), Roche, Eli Lilly and Company ("Lilly"), Alexion Pharmaceuticals, Inc. (together with its affiliates, "Alexion"), Boehringer Ingelheim International GmbH ("BI"), and Alnylam Pharmaceuticals, Inc. ("Alnylam"). Between Dicerna and its collaborative partners, the Company currently has more than 20 active discovery, preclinical, or clinical programs focused on cardiometabolic, viral, chronic liver, and complement-mediated diseases, as well as neurodegenerative diseases and pain.

COVID-19

On March 11, 2020, the World Health Organization declared the spread of the novel coronavirus ("COVID-19") a pandemic. The global spread of COVID-19 has created significant volatility, uncertainty, and economic disruption worldwide. Governments in affected regions have implemented, and may continue to implement, safety precautions which include quarantines, travel restrictions, business closures, and other public health safety measures.

Throughout 2020 and into 2021, Dicerna was impacted by mandatory work from home edicts directed by local governments in the jurisdictions in which the Company operates. However, essential work exemptions continued to permit critical research and development and laboratory activities for limited personnel. Those exemptions enabled some continued discovery research and activities supporting the Company's collaborative agreements and its own programs. Externally, the COVID-19 pandemic has resulted in some challenges in reserving slots for preclinical studies and accessing non-human primates for such studies, as well as slower enrollment in the Company's clinical trials. Dicerna has undertaken efforts to mitigate potential impacts to our business including those related to conducting clinical trials and managing our supply chain. The Company continues to be alert to the potential for disruptions that could arise from COVID-19 or its variants and monitors the Food and Drug Administration's ("FDA") and other health authorities' guidance for the conduct of clinical trials during this time.

Current supply of Dicerna's investigational medicines is sufficient to support ongoing and planned clinical trials. Based on current evaluations, Dicerna's supply chains continue to appear intact to meet at least the next 18 months of clinical, nonclinical, commercial, and chemistry, manufacturing, and control ("CMC") supply demands across all programs. The Company has undertaken efforts to mitigate potential future impacts to the supply chain by increasing its stock of critical starting materials required to meet its needs and its collaborative partners' needs through 2022 and by identifying and engaging alternative suppliers. The Company continues to be alert to the potential for disruptions that could arise from COVID-19 or its variants, including on account of United States ("U.S.") government utilization of its Defense Production Act authorities, and remains in close contact with suppliers.

It is difficult to predict what the lasting impact of the pandemic will be, and what the impact might be if the Company or any of the third parties with whom it engages were to experience additional shutdowns or other prolonged business disruptions. The Company's ability to conduct its business in the manner and on the timelines presently planned could have a material adverse impact on the Company's business, results of operations, and financial condition. In addition, depending on the duration and impact of the recurrence or resurgence of COVID-19 cases or continued evolution of further strains of COVID-19 or its variants, and depending on where the infection rates are highest, and including the ability of regulators to continue ensuring the timely review and approval of applications, the Company's business, results of operations, and financial condition may be negatively impacted. The Company will continue to monitor developments as it deals with the disruptions and uncertainties relating to the COVID-19 pandemic.

Basis of presentation

These condensed consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP") along with the rules and regulations of the Securities and Exchange Commission for interim financial information, and include the accounts of Dicerna Pharmaceuticals, Inc. and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation. The year-end condensed consolidated balance sheet data were derived from audited financial statements but do not include all disclosures required by GAAP to constitute a complete set of financial statements. These condensed consolidated financial statements have been prepared on the same basis as the Company's annual consolidated financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments necessary for a fair statement of the Company's financial position at June 30, 2021 and its results of operations, changes in stockholders' equity, and cash flows for the interim periods ended June 30, 2021 and 2020. These unaudited condensed consolidated interim financial statements should be read in conjunction with the Company's audited consolidated financial statements and notes thereto included in the Company's Annual Report on Form 10-K for the year ended December 31, 2020. The results of operations for the three and six months ended June 30, 2021 are not necessarily indicative of the results to be expected for the year ending December 31, 2021, for any other interim period, or for any other future year.

Significant judgments and estimates

The preparation of condensed consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the Company's condensed consolidated financial statements, as well as the revenues and expenses incurred during the reporting periods. On an ongoing basis, the Company evaluates judgments and estimates, including those related to revenue recognition, deferred income, stock-based compensation, the derivative liability, and accrued expenses. The Company bases its estimates on historical experience and on various other factors that the Company believes are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results could differ materially from those estimates.

Recent accounting pronouncements

In December 2019, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2019-12, *Simplifying the Accounting for Income Taxes*, amending accounting guidance that simplifies the accounting for income taxes as part of its initiative to reduce complexity in the accounting standards. The amendments eliminate certain exceptions related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period, and the recognition of deferred tax liabilities for outside basis differences. The amendments also clarify and simplify other aspects of the accounting for income taxes. For public business entities, ASU 2019-12 is required to be adopted effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2020. The Company adopted ASU 2019-12 on January 1, 2021 and it did not have a material impact on its financial statements or related disclosures.

Summary of significant accounting policies

There have been no changes to the significant accounting policies disclosed in the Company's most recent Annual Report on Form 10-K.

2. NET LOSS PER SHARE

The Company computes basic net loss per common share by dividing net loss by the weighted average number of common shares outstanding. In periods of net income, the Company's accounting policy includes allocating a proportional share of net income to participating securities, as 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"). Participating securities have the effect of diluting both basic and diluted earnings per share during periods of income. During periods when the Company incurs a net loss, the Company does not allocate a loss to participating securities because they have no contractual obligation to share in the losses of the Company. The Company computes diluted net loss per common share after giving consideration to the dilutive effect of stock options and nonvested restricted stock units that are outstanding during the period, except where such non-participating securities would be anti-dilutive.

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

	JUNE 30, 2021	JUNE 30, 2020
Options to purchase common stock	14,307,555	15,109,939
Nonvested restricted stock units	1,221,426	887,355
Total	15,528,981	15,997,294

3. HELD-TO-MATURITY INVESTMENTS

A summary of the Company's held-to-maturity investments is presented below:

	JUNE 30, 2021			
DESCRIPTION	AMORTIZED COST	GROSS UNREALIZED HOLDING GAINS	GROSS UNREALIZED HOLDING LOSSES	FAIR VALUE
U.S. Treasury securities maturing in one year or less	$ 371,755	$ 39	$ (13)	$ 371,781
U.S. Treasury securities maturing in greater than one year	116,599	—	(34)	116,565
Total	$ 488,354	$ 39	$ (47)	$ 488,346

	DECEMBER 31, 2020			
DESCRIPTION	AMORTIZED COST	GROSS UNREALIZED HOLDING GAINS	GROSS UNREALIZED HOLDING LOSSES	FAIR VALUE
U.S. Treasury securities maturing in one year or less	$ 442,820	$ 163	$ (12)	$ 442,971

The Company's policy is not to measure an allowance for credit losses for interest receivable and to write off any uncollectible interest receivable as a reversal of interest income in the period in which it determines the interest will not be collected. The Company did not write off any interest receivable during the three and six months ended June 30, 2021 and 2020.

The contractual terms of these investments do not permit the issuer to settle the securities at a price less than the amortized cost bases of the investments. The Company does not intend to sell its investments and has the intent and ability to hold its investments until they mature.

4. FAIR VALUE MEASUREMENTS

A summary of the Company's assets and liabilities that are measured or disclosed at fair value on a recurring basis is presented below:

DESCRIPTION	JUNE 30, 2021 TOTAL FAIR VALUE	LEVEL 1	LEVEL 2	LEVEL 3
Financial assets				
Cash equivalents				
Money market funds	$ 220,835	$ 220,835	$ —	$ —
Held-to-maturity investments				
U.S. Treasury securities	488,346	—	488,346	—
Restricted cash equivalents				
Money market funds	5,618	5,618	—	—
Total financial assets	$ 714,799	$ 226,453	$ 488,346	$ —
Financial liabilities				
Derivative liability	$ 7,750	$ —	$ —	$ 7,750
Total financial liabilities	$ 7,750	$ —	$ —	$ 7,750

DESCRIPTION	DECEMBER 31, 2020 TOTAL FAIR VALUE	LEVEL 1	LEVEL 2	LEVEL 3
Financial assets				
Cash equivalents				
Money market funds	$ 126,006	$ 126,006	$ —	$ —
Held-to-maturity investments				
U.S. Treasury securities	442,971	—	442,971	—
Restricted cash equivalents				
Money market funds	6,362	6,362	—	—
Total financial assets	$ 575,339	$ 132,368	$ 442,971	$ —
Financial liabilities				
Derivative liability	$ 6,000	$ —	$ —	$ 6,000
Total financial liabilities	$ 6,000	$ —	$ —	$ 6,000

The Company's cash equivalents and restricted cash equivalents, which are held in money market funds, are classified within Level 1 of the fair value hierarchy because they are valued using quoted prices in active markets as of June 30, 2021 and December 31, 2020. Restricted cash equivalents represent money market investments which secure letters of credit established in connection with the Company's facility leases.

The Company's held-to-maturity investments bore interest at the prevailing market rates for instruments with similar characteristics and therefore the amortized cost approximated fair value. These financial instruments were classified within Level 2 of the fair value hierarchy because the inputs to the fair value measurements were valued using observable inputs as of June 30, 2021 and December 31, 2020.

The Company does not enter into derivative financial instruments for speculative or trading purposes. The Company has a derivative liability associated with certain contingent payments under our collaboration agreement with Alnylam, which is classified within Level 3 of the fair value hierarchy because the fair value utilizes unobservable inputs for which there is no market data and therefore requires the Company to develop its own assumptions. Such assumptions include the probability of success of development, the probability that Alnylam exercises its commercialization option, the timing of regulatory approval and the first commercial sale, and the volume of sales.

The following table presents a rollforward of activity associated with the derivative liability during the six months ended June 30, 2021:

	CONTINGENT PAYMENT DERIVATIVE LIABILITY
Balance, January 1, 2021	$ (6,000)
Expense recognized in other (expense) income due to remeasurement of fair value of the liability	(1,500)
Balance, March 31, 2021	(7,500)
Expense recognized in other (expense) income due to remeasurement of fair value of the liability	(250)
Balance, June 30, 2021	$ (7,750)

It is our policy to recognize transfers between levels of the fair value hierarchy, if any, at the end of the reporting period; however, there have been no such transfers during the periods presented.

As of June 30, 2021 and December 31, 2020, the Company's contract receivables, accounts payable, and accrued expenses approximated their estimated fair values because of the short-term nature of these financial instruments.

5. PREPAID EXPENSES AND OTHER CURRENT ASSETS

Prepaid expenses and other current assets consist of the following:

	JUNE 30, 2021	DECEMBER 31, 2020
Prepaid clinical, contract research, and manufacturing costs	$ 11,107	$ 9,651
Interest receivable	1,868	1,345
Prepaid insurance	1,749	817
Other prepaid expenses and other current assets	5,656	2,590
Prepaid expenses and other current assets	$ 20,380	$ 14,403

6. COLLABORATIVE RESEARCH AND LICENSE AGREEMENTS

Alnylam collaboration and patent cross-license agreements

Background

On April 3, 2020, the Company and Alnylam (collectively, the "parties") entered into a Collaboration and License Agreement (the "A1AT Agreement") and a Patent Cross License Agreement (the "PH Agreement"). Pursuant to the A1AT Agreement, Dicerna will lead efforts on investigational RNAi therapeutics for the treatment of alpha-1 antitrypsin ("AAT") deficiency ("AATD")-associated liver disease ("AATLD"). Pursuant to the PH Agreement, the parties completed a cross-license of their respective intellectual property for Alnylam's lumasiran and Dicerna's nedosiran investigational programs for the treatment of primary hyperoxaluria ("PH"). No upfront cash consideration was exchanged in either transaction.

Pursuant to the A1AT Agreement, Alnylam's AAT product (ALN-AAT02, or the "Alnylam Product") and Dicerna's AAT product (belcesiran, or the "Dicerna Product") were to be explored for the treatment of AATLD. Under the A1AT Agreement, the Company obtained an exclusive worldwide license to Alnylam's intellectual property to exploit the Alnylam Product. Dicerna assumed responsibility for the development of both the Alnylam Product and the Dicerna Product at its cost. Dicerna selected belcesiran to advance in development for the treatment of patients with AATLD. At the completion of Phase 3, Alnylam has the no-cost opportunity to opt-in to commercialize belcesiran in countries outside the U.S. where it already has a commercialization infrastructure in place (the "Commercialization Option"). If Alnylam exercises its Commercialization Option, the parties will share future development costs. Further, each party will pay tiered royalties to the other party based on a percentage of net product sales generated in its territory ranging from low single-digits to high teens. In the event Alnylam waives its Commercialization Option, the Company will retain worldwide rights to commercialize belcesiran in exchange for payments upon the satisfaction of certain milestones, up to an aggregate of $45.0 million, and royalties will be payable to Alnylam based on net product sales in the low to mid-single-digits. As a result of these uncertain payments the Company may owe to Alnylam, the Company has recorded a derivative liability on the condensed consolidated balance sheets as of June 30, 2021 and December 31, 2020. The A1AT Agreement is subject to customary termination provisions, and the Company may terminate the A1AT Agreement at any time without cause following the notice period described in the A1AT Agreement.

Pursuant to the PH Agreement, the parties granted to each other a perpetual non-exclusive cross-license to their respective intellectual property related to their respective PH treatment investigational programs to ensure that each party has the freedom to develop and

commercialize its respective product with Alnylam's lumasiran targeting glycolate oxidase ("GO") for the treatment of PH type 1 and Dicerna's nedosiran targeting lactate dehydrogenase A ("LDHA") for the treatment of PH types 1, 2, and 3. Each party will have sole discretion concerning the research and development of its products in the field. In exchange for the license, Alnylam is required to pay mid- to high-single-digit royalties to Dicerna based on global net sales of lumasiran and Dicerna is required to pay low-single-digit royalties to Alnylam on global net sales of nedosiran. The PH Agreement cannot be terminated by either party for the other party's breach. However, either party may terminate the PH Agreement or may reduce the royalty payable to the other party upon a patent-related challenge by the other party unless the challenge is withdrawn and no longer pending within the time periods specified in the PH Agreement. Further, the PH Agreement will terminate upon the expiration of the last-to-expire patent rights licensed thereunder.

In April 2021, pursuant to an agreement with Royalty Pharma plc ("Royalty Pharma"), the Company received a $180.0 million upfront payment from the sale of Dicerna's royalty interest in Alnylam's net sales of OXLUMO (lumasiran). The upfront payment was recorded as deferred income upon receipt. Under this agreement, the Company is also eligible to receive up to $60.0 million in contingent sales-based milestone payments. Refer to Note 7 - Royalty Pharma Financing for further details.

Accounting Analysis

The Company determined that the A1AT Agreement and the PH Agreement represent separate agreements for accounting purposes, as the transactions have different commercial objectives, the consideration under each contract is not dependent upon the price or performance of the other contract, and the goods or services under each contract are separate performance obligations.

A1AT Agreement

The Company concluded that the A1AT Agreement was within the scope of Accounting Standards Codification ("ASC") 606, *Revenue from Contracts with Customers*, as the provision of research and development services is considered an output of the entity's ordinary activities in exchange for consideration.

The Company identified a single performance obligation under the A1AT Agreement, which consists of the provision of certain nonclinical and clinical services through the completion of the Phase 1 clinical trial for any product.

The Company determined that the transaction price at inception of the A1AT Agreement consists of non-cash consideration in the form of the license received from Alnylam. The Company determined that the fair value of the non-cash consideration (the license received from Alnylam) is insignificant given the early-stage development status of the Alnylam Product and the related risks associated with developing a commercial product. The sales-based royalties that Dicerna may be entitled to receive in the event that Alnylam exercises its Commercialization Option have been excluded from the transaction price and will be recognized only if Alnylam exercises its Commercialization Option and the related sales occur.

As described above, Dicerna may be required to pay contingent milestones and royalties to compensate Alnylam for the license provided under the agreement. Given the uncertainty associated with these contingent payments, the Company established a derivative liability for these payments and recognized $6.0 million of other expense in the period ended December 31, 2020. In the six months ended June 30, 2021, the Company recognized an additional $1.75 million of other expense associated with this liability.

The Company has recorded development costs incurred under the A1AT Agreement as research and development expenses in the Company's condensed consolidated statement of operations.

PH Agreement

The Company concluded that the PH Agreement is within the scope of ASC 610, *Other Income – Gains and Losses from the Derecognition of Nonfinancial Assets*, as the exchange of non-exclusive licenses is considered an exchange of non-financial assets outside the ordinary scope of business. Pursuant to ASC 610-20, the Company applied the guidance in ASC 606 to determine if a contract exists, identify the distinct non-financial assets, and determine when control transfers and, therefore, when to derecognize the asset. Additionally, the Company applied the measurement principles of ASC 606 to determine the amount of consideration, if any, to include in the calculation of the gain or loss for the non-financial asset.

The Company determined that it transferred control of a non-financial asset (the non-exclusive license granted to Alnylam) at contract inception. Applying the non-cash consideration guidance in ASC 606, the Company further determined that the fair value of the non-financial asset received (the non-exclusive license from Alnylam) was insignificant. Therefore, the Company concluded that no gain or loss would be recorded related to the PH Agreement at contract inception.

The Company has recorded costs related to its PH program as research and development expenses in the Company's condensed consolidated statement of operations.

Novo collaboration and share purchase agreements

Background

On November 15, 2019, Dicerna and Novo entered into a Collaboration and License Agreement (the "Novo Collaboration Agreement"). Under the terms of the Novo Collaboration Agreement, the Company and Novo seek to use GalXC to explore more than 30 gene targets associated with liver disease with the goal of delivering multiple clinical candidates for disorders including chronic liver disease, non-alcoholic steatohepatitis ("NASH"), type 2 diabetes, obesity, and rare diseases. The Company will conduct and fund discovery and preclinical development to clinical candidate selection for each liver cell target. Novo will be responsible for all further development and the commercialization of each candidate selected for development, with the Company manufacturing clinical candidates selected for Phase 1-related clinical development, subject to reimbursement for its manufacturing costs. In addition, the Company will assist Novo with the Investigational New Drug ("IND") filing for the first development candidate. The Company also retains the ability to opt in to co-development of a total of two programs during clinical development in Phases 1-3, subject to limitations in the event of a change in control. If the Company exercises a co-development option, it also has an option to co-promote the product in the United States, subject to limitations in the event of a change in control of the Company. Additionally, the Company may lead the development and commercialization of two programs targeting orphan liver diseases, with Novo retaining the ability to opt in to both programs in Phases 1-3. The Company and Novo will share in profits and losses for the Company's orphan liver and Novo products should both parties elect to co-develop.

The Company is working exclusively with Novo during the research collaboration period on the discovery, research, development, and commercialization of hepatocyte targets subject to certain exclusions including those targets subject to the Company's existing partnerships, and Novo is, during a specified discovery period, working exclusively with the Company in any new research and development of compounds and products directed to collaboration targets using small interfering RNA ("siRNA") conjugated to the sugar N-acetyl-D-galactosamine ("GalNAc") to reduce the expression of specific target genes in the liver. Under the Novo Collaboration Agreement, the Company is providing Novo with exclusive and non-exclusive licenses and manufacturing support to enable Novo to commercialize products derived from or containing compounds developed pursuant to such agreement.

Under the terms of the Novo Collaboration Agreement, Novo paid the Company an upfront payment of $175.0 million, which was subject to delivery of target information, in January 2020. The Company is also eligible to receive an additional $75.0 million ($25.0 million at the end of each of the first three years of the Novo Collaboration Agreement), contingent upon the Company delivering GalXC molecules for a defined number of targets, and additional payments totaling up to approximately $357.5 million per target upon achievement of specified development, regulatory, and commercial milestones. In addition, Novo will pay the Company mid-single-digits to mid-teens royalties on product sales on a country-by-country and product-by-product basis until the later of 10 years after the date of first commercial sale of each product in such country, expiration of specified patent rights in such country, or the expiration of specified regulatory exclusivity in such country for GalXC products, subject to royalty step-down provisions set forth in the agreement.

In connection with the Novo Collaboration Agreement, the Company and Novo entered into the Novo Share Issuance Agreement on November 15, 2019, pursuant to which Novo purchased 2,279,982 shares (the "Novo Shares") of the Company's common stock, par value $0.0001 per share ("Common Stock"), at a purchase price of $21.93 per share, for an aggregate purchase price of approximately $50.0 million.

During the fourth quarter of 2020, Novo nominated its first candidate under the Novo Collaboration Agreement. Pursuant to the agreement, upon achievement of proof of principle of the first nominated candidate, Dicerna earned a $2.5 million milestone, which the Company received in February 2021. Also during the fourth quarter of 2020, Novo confirmed that Dicerna met its annual obligation to deliver GalXC molecules for a defined number of targets for the first year of the Novo Collaboration Agreement, entitling the Company to a $25.0 million payment, which the Company received in February 2021.

Accounting Analysis

The Novo Collaboration Agreement and the Novo Share Issuance Agreement (collectively, "the Novo Agreements") were executed on the same date and negotiated as a package. Management therefore concluded that the Novo Agreements are to be combined for accounting purposes and concluded that Novo is a customer in this arrangement pursuant to the revenue recognition guidance.

The Company identified contract promises under the agreement for the license of intellectual property and know-how rights for selected gene targets and research and development services to develop a clinical candidate for each selected gene target, including manufacturing activities. The Company may also be required to provide research and development services for an unspecified number of targets, with the goal of the collaboration being to develop clinical candidates for each of the selected gene targets. The Company determined that the license and research and development services were not capable of being distinct or distinct within the context of the contract. The research and development services to be provided by Dicerna are specialized in nature, specifically with respect to the Company's therapeutic expertise related to RNAi and the Company's GalXC conjugates. In addition, there is an interdependent

relationship between the contract promises. As such, the Company concluded that there is a single identified combined performance obligation consisting of a license and research and development services.

The Company may be required to perform certain additional services after Novo's nomination of a development candidate. These services include Phase 1-related activities, such as manufacturing through the approval of an IND application for a development candidate, research and development activities to support the filing of an IND application for the first development candidate, and other development services to support Novo's development activities related to any development candidates. The Company will be reimbursed by Novo for these additional services. Because the provision of these additional goods and services are conditional on Novo electing to nominate a development candidate, the Company has concluded that these goods and services represent customer options and are not considered performance obligations.

The total transaction price for the Novo Agreements is $256.7 million, consisting of the total $175.0 million upfront compensation, the $75.0 million additional aggregate payments described above (payable in equal annual payments of $25.0 million), a $4.2 million premium on the sale of shares under the Novo Share Issuance Agreement, and a $2.5 million milestone earned in the fourth quarter of 2020 for achieving proof of principle for the first candidate. The Company applied equity accounting guidance to measure the $45.8 million recorded in equity upon the issuance of the shares. The upfront payment of $175.0 million was payable to the Company upon the delivery of a bioinformatics package and mapping plan for at least one of the initial targets selected by Novo and was paid in January 2020. If the Novo Collaboration Agreement is terminated prior to the third anniversary of its effective date, the Company is entitled to 80% of the outstanding and unearned annual payments. The Company assumed that the mapped targets will be delivered and that the contract will not be canceled. The Company has experience with mapping targets, and therefore, concluded that such amount does not need to be constrained. Accordingly, the Company included the $75.0 million of additional payments in the transaction price.

The Company used the most likely amount method to estimate variable consideration and estimated that the most likely amount for each potential future preclinical, development, and regulatory variable consideration milestone payment under this agreement was zero, as the achievement of those milestones is uncertain and highly susceptible to factors outside of the Company's control. Accordingly, all potential future milestones were excluded from the transaction price. Management reevaluates the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur and adjusts the transaction price as necessary. Sales-based royalties, including milestone payments based on the level of sales, were also excluded from the transaction price, as the license is deemed to be the predominant item to which the royalties relate. The Company will recognize such revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

Revenue associated with the performance obligation is being recognized as services are provided using a cost-to-cost measure of progress method. The transfer of control occurs over time, as the Company's performance does not create an asset with alternative use, and the Company has an enforceable right to payment for performance completed to date. In management's judgment, this input method is the best measure of progress towards satisfying the performance obligation and reflects a faithful depiction of the transfer of goods and services.

The aggregate amount of the transaction price allocated to the Company's unsatisfied or partially unsatisfied performance obligations under the Novo Collaboration Agreement at June 30, 2021 was $229.6 million. As of June 30, 2021, the Company expected to recognize the balance of deferred revenue over the remaining portion of the five-year research term, or four years, which may be extended for up to two years.

Roche collaboration agreement

Background

On October 30, 2019, the Company and Roche entered into a Collaboration and License Agreement (the "Roche Collaboration Agreement"). Under the terms of the Roche Collaboration Agreement, the Company and Roche seek to progress RG6346, the companies' investigational therapy in clinical development, toward worldwide development and commercialization. The Roche Collaboration Agreement also provides an option for the companies to collaborate in the discovery, development, and commercialization of oligonucleotide therapeutics intended for the treatment of hepatitis B virus ("HBV").

The Roche Collaboration Agreement requires that Dicerna complete the ongoing Phase 1 clinical trial, including additional Phase 1 cohorts that were requested by Roche for which Roche will reimburse the Company for the cost of the additional cohorts. Roche will lead the post-Phase 1 development and commercialization of the RG6346 program. Roche also had until receipt of interim Phase 1 data from the RG6346 Phase 1 study (but no later than December 31, 2020) to initiate a research and development collaboration with the Company to pursue up to five targets selected by Roche, (each a "Selected Target"), which are intended primarily to treat HBV. Under an amendment to the Roche Collaboration Agreement in June 2020, Roche and Dicerna agreed to extend the date for nomination of targets from December 31, 2020 to January 15, 2021, subject to further potential extension by the parties due to the

COVID-19 global pandemic shutdowns. Under an additional amendment to the Roche Collaboration Agreement in May 2021, Roche and Dicerna further agreed to extend the date for nomination of the targets to June 15, 2021. In April 2020, Roche nominated the first target, and as of the three months ended June 30, 2021, Roche had nominated three of the up to five targets under the research and development portion of the Roche Collaboration Agreement. Under the terms of the Roche Collaboration Agreement, the goal of such research and development collaboration will be to select compounds developed by the Company or Roche for Roche's continued development and commercialization. The Company's and Roche's research and early development organizations will work exclusively with each other during the research and development collaboration period on the discovery, research, and development of such targets selected by Roche, which includes the performance of certain services by Dicerna. Under the Roche Collaboration Agreement, the Company is providing Roche with exclusive and non-exclusive licenses to support Roche's activities and to enable Roche to commercialize products derived from or containing compounds developed pursuant to such agreement.

Under the terms of the Roche Collaboration Agreement, Roche paid the Company a non-refundable upfront payment of $200.0 million in January 2020. The Company is also eligible to receive additional payments totaling up to approximately $1.47 billion, which includes payments upon achievement of specified development, regulatory, and commercial milestones. In addition, Roche will pay the Company up to mid-teens percent royalties on worldwide product sales. Royalties are payable until the later of 10 years after first commercial sale of each product in a country, expiration of patent rights in a country, or for products containing RG6346 in a given country, the expiration of data or regulatory exclusivity, subject to certain royalty step-down provisions set forth in the agreement. In addition, the Company has an option to co-fund the development of products under the agreement and, if exercised, receive high-twenties to mid-thirties royalty rates on net sales of products in the U.S. If the Company exercises the co-funding option, it also has an option to co-promote products containing RG6346 in the U.S.

Accounting Analysis

The Company concluded that Roche is a customer in this arrangement pursuant to the revenue recognition guidance. The Company identified contract promises under the agreement for (i) the license of intellectual property and know-how rights related to the lead compound, (ii) research and development services to complete the Phase 1 study associated with the lead compound, (iii) lead compound transfer activities, (iv) manufacturing of clinical supply for the lead compound Phase 1 study, and (v) Roche's option to receive additional goods and services related to the research and development collaboration. The Company determined that the Roche Collaboration Agreement contains two performance obligations consisting of: (i) a combined performance obligation that includes a license, related development and manufacturing services to complete the Phase 1 study, and manufacturing obligations through the completion of the Phase 1 study related to the lead compound (the "RG6346 Performance Obligation"), and (ii) a material right to enter into a research and development collaboration to develop additional targets. While evaluating contract promises to determine whether each was capable of being distinct and distinct within the context of the contract, management considered the specialized nature of the services to be provided by Dicerna, specifically with respect to the Company's therapeutic expertise related to RNAi and the Company's GalXC conjugates and the interdependent relationship between the contract promises. As such, the Company concluded that the promises of the license and research and development services related to the lead compound were not distinct from each other. Accordingly, these promises were combined into one performance obligation, the RG6346 Performance Obligation. Upon Roche's exercise of its option to enter into the research and development collaboration for which no additional consideration was received, Roche had the right to nominate up to five additional targets. For each target nominated, Roche received a license to the Selected Target, for which the Company will perform research services through clinical candidate selection. The Company concluded that, upon Roche's nomination of a target, the license and related research services through clinical candidate selection for each Selected Target represents a combined performance obligation, which is separate from the RG6346 Performance Obligation. The Company is not required to perform services on more than three Selected Targets at any time. Roche also had the right to replace up to three Selected Targets if a clinical candidate could not be identified during the research term.

The total transaction price for the Roche Collaboration Agreement is $232.1 million, consisting of the $200.0 million upfront payment, a $25.0 million milestone payment associated with Roche's initiation of RG6346 in a Phase 2 combination trial, and the estimated reimbursement from Roche related to the additional cohorts. The Company used the most likely amount method to estimate the amount of reimbursement, which was considered variable consideration. As reimbursement will be made as the Company performs the related services, the Company concluded that such amount does not need to be constrained, and therefore, included the full amount of the estimated reimbursement by Roche in the transaction price.

The Company also estimated that the most likely amount for each potential future development and regulatory variable consideration milestone payment under this agreement was zero at contract inception, as the achievement of those milestones was uncertain and highly susceptible to factors outside of the Company's control. Accordingly, all potential future milestones were initially excluded from the transaction price. Management reevaluates the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur and adjusts the transaction price as necessary. Sales-based royalties, including milestone payments based on the level of sales, were also excluded from the transaction price, as the license is deemed to be the predominant item to which the royalties relate. The Company will recognize such revenue at the later of (i) when the related sales

occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

The Company allocated the current $232.1 million transaction price to the performance obligations on a relative standalone selling price basis. The Company estimated the standalone selling price for the lead compound performance obligation using the adjusted market assessment approach, whereby the Company adjusted comparable third-party transactions to reflect the stage of development of the Company's asset. To determine the estimated standalone selling price of the material right, the Company estimated the standalone selling price of the underlying performance obligations included in the material right and estimated the probability of Roche exercising such underlying performance obligations. The Company concluded that the research and development collaboration material right contained (i) five material rights to receive a selected target license and related research and development services, and (ii) three material rights to receive a replacement selected target license and related research and development services. Upon the nomination of a target, the Selected Target license and related research services through clinical candidate selection are accounted for as a combined performance obligation. The value of the material right related to the Selected Target is included in the transaction price for the combined performance obligation. The variable consideration related to the reimbursement from Roche for the additional Phase 1 cohorts and any milestones and royalties that are achieved will be allocated specifically to the lead compound performance obligation, as this variable consideration relates specifically to the Company's satisfaction of the lead compound performance obligation and such allocation has been determined to be consistent with the allocation objective of the revenue recognition guidance.

Revenue associated with the lead compound performance obligation is recognized as services are provided using a cost-to-cost measure of progress method. The transfer of control occurs over time, as the Company's performance does not create an asset with alternative use, and the Company has an enforceable right to payment for performance completed to date. In management's judgment, this input method is the best measure of progress towards satisfying the performance obligation and reflects a faithful depiction of the transfer of goods and services. The transaction price allocated to the research and development collaboration material right is recognized based on the timing of recognition of the underlying performance obligations that comprise the material right, or upon expiry of the material right if such right is not exercised.

The aggregate amount of the transaction price allocated to the Company's unsatisfied or partially unsatisfied performance obligations under the Roche Collaboration Agreement at June 30, 2021 was $122.1 million. As of June 30, 2021, the Company expects to recognize the balance of deferred revenue during the research term of up to five years.

Lilly collaboration and share purchase agreements

Background

On October 25, 2018, the Company entered into a Collaboration and License Agreement with Lilly (the "Lilly Collaboration Agreement") for the discovery, development, and commercialization of potential new medicines in the areas of cardiometabolic disease, neurodegenerative diseases, and pain. Under the terms of the Lilly Collaboration Agreement, the Company and Lilly will use the Company's proprietary GalXC RNAi technology to progress new drug targets toward clinical development and commercialization. In addition, the Company and Lilly will collaborate on non-liver (i.e., extrahepatic) tissues, including neural tissues.

The Company will work exclusively with Lilly in the neurodegenerative disease and pain fields, with the exception of mutually agreed upon orphan indications. Additionally, the Company will work exclusively with Lilly on select targets in the cardiometabolic field. Under the Lilly Collaboration Agreement, the Company will provide Lilly with exclusive and non-exclusive licenses to support the companies' activities and to enable Lilly to commercialize products derived from or containing compounds developed pursuant to such agreement. The Lilly Collaboration Agreement provides for three initially named hepatocyte targets, and the Company and Lilly developed research programs with the goal of researching and developing multiple lead candidates directed to each of these initial targets. The Lilly Collaboration Agreement contemplates in excess of ten targets.

Lilly paid the Company a non-refundable upfront payment of $100.0 million. The Company is also eligible to receive up to $350.0 million per target in development and commercialization milestones, in addition to a $5.0 million payment, which will become due for each of the extrahepatic targets when a product candidate achieves proof of principle in an animal model. In addition, the Company is eligible to earn mid-single- to low-double-digit royalties on product sales on a country-by-country and product-by-product basis until the later of expiration of patent rights in a country, the expiration of data or regulatory exclusivity in such country, or 10 years after the first product sale in such country, subject to certain royalty step-down provisions set forth in the agreement.

Simultaneously with the entry into the Lilly Collaboration Agreement, the Company and Lilly entered into a Share Purchase Agreement (the "Lilly Share Issuance Agreement"), pursuant to which Lilly purchased 5,414,185 shares of the Company's common stock at $18.47 per share, for an aggregate purchase price of $100.0 million. The Lilly Share Issuance Agreement is to be combined with the Lilly Collaboration Agreement (together, the "Combined Agreements") for accounting purposes.

During the fourth quarter of 2020, Dicerna achieved a milestone associated with the first filing of an IND application for LY3561774, targeting the *ANGPTL3* gene for the treatment of dyslipidemia, with the FDA, entitling the Company to a $10.0 million payment. The Company received this payment in the fourth quarter of 2020.

In February 2021, Lilly notified us of their decision to extend for an additional year the initial research collaboration term for the extrahepatic targets subject to the Lilly Collaboration Agreement. Under the agreement between the companies, Lilly has the option to extend the three-year initial research collaboration term for these extrahepatic targets for up to three consecutive one-year periods. This first extension allows the research program for these extrahepatic targets under the collaboration between the two companies to continue through October 2022.

During the second quarter of 2021, the FDA accepted the IND application filed by Lilly for LY3819469, targeting the *LPA* gene as a potential treatment for cardiometabolic diseases, triggering a $10.0 million payment to Dicerna. The Company received this payment in the second quarter of 2021.

Accounting Analysis

The Company concluded that Lilly is a customer in this arrangement. As such, the element of the arrangement unrelated to the issuance of the shares falls within the scope of the revenue recognition guidance. The Company identified contract promises under the Combined Agreements for licenses of intellectual property and know-how rights, associated research and development services for targets and for exploration of new applications of the Company's RNAi technology to non-liver targets, and participation on a joint steering committee. The Company determined that the contract promises were not separately identifiable and were not distinct or distinct within the context of the contract due to the specialized nature of the services to be provided by Dicerna, specifically with respect to the Company's therapeutic expertise related to RNAi and the Company's GalXC conjugates, and the interdependent relationship between the contract promises. As such, the Company concluded that there was a single identified combined performance obligation. The total transaction price for the Combined Agreements is $168.7 million, consisting of the total $100.0 million upfront compensation, $48.7 million premium on the sale of shares under the Lilly Share Issuance Agreement, and $10.0 million milestones for the achievement of each of the IND filings. The Company applied equity accounting guidance to measure the $51.3 million recorded in equity upon the issuance of the shares.

The Company used the most likely amount method to estimate variable consideration and estimated that the most likely amount for each potential future development milestone payment under this agreement was zero, as the achievement of those milestones is uncertain and highly susceptible to factors outside of the Company's control. Accordingly, all potential future milestones were excluded from the transaction price. Management reevaluates the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur and adjusts the transaction price as necessary. Sales-based royalties, including milestone payments based on the level of sales, were also excluded from the transaction price, as the license is deemed to be the predominant item to which the royalties relate. The Company will recognize such revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

Revenue associated with the performance obligation will be recognized as services are provided using a cost-to-cost measure of progress method. The transfer of control occurs over time and, in management's judgment, this input method is the best measure of progress towards satisfying the performance obligation and reflects a faithful depiction of the transfer of goods and services.

The aggregate amount of the transaction price allocated to the Company's unsatisfied or partially unsatisfied performance obligations under the Lilly Collaboration Agreement at June 30, 2021 was $93.0 million. As of June 30, 2021, the Company expected to recognize the majority of this amount over the remaining research term of the agreement, which is expected to extend through the fourth quarter of 2022.

Alexion collaboration and equity agreements

Background

On October 22, 2018, the Company and Alexion entered into a Collaborative Research and License Agreement (the "Alexion Collaboration Agreement"). The Alexion Collaboration Agreement is for the joint discovery and development of RNAi therapies for complement-mediated diseases. The Company and Alexion will collaborate on the discovery and development of two subcutaneously delivered GalXC candidates, currently in preclinical development, for the treatment of complement-mediated diseases with potential global commercialization by Alexion. The Company will lead the joint discovery and research efforts through the preclinical stage, and Alexion will lead development efforts beginning with Phase 1 studies. The Company will be responsible for manufacturing of the GalXC candidates through the completion of Phase 1, and certain related costs will be paid by Alexion. Alexion will be solely responsible for the manufacturing of any product candidate subsequent to the completion of Phase 1. The Alexion Collaboration Agreement provides Alexion with exclusive worldwide licenses as well as development and commercial rights to the GalXC RNAi

molecules developed in the collaboration in exchange for development and approval-related milestones, sales milestones, and royalties on future product sales.

Alexion paid the Company a non-refundable upfront payment of $22.0 million. The Alexion Collaboration Agreement also provides for potential additional payments to the Company of up to $600.0 million from proceeds from target option exercises and development and sales milestones, as defined in the agreement, which includes: (i) option exercise fees of up to $20.0 million, representing $10.0 million for each of the targets selected; (ii) development milestones of up to $105.0 million for each product; and (iii) aggregate sales milestones of up to $160.0 million. Alexion also agreed to pay the Company mid-single- to low-double-digit royalties on potential product sales on a country-by-country, product-by-product basis until the later of the expiration of patent rights in a country, the expiration of market or regulatory exclusivity in such country, or 10 years after the first product sale in such country, subject to certain royalty step-down provisions set forth in the agreement.

Simultaneously with the entry into the Alexion Collaboration Agreement, the Company and Alexion entered into a Share Purchase Agreement (the "Alexion Share Issuance Agreement"), pursuant to which Alexion purchased 835,834 shares of the Company's common stock at $17.95 per share at issuance, for an aggregate purchase price of $15.0 million. Management concluded that the Alexion Share Issuance Agreement was to be combined with the Alexion Collaboration Agreement (together, the "Alexion Agreements") for accounting purposes. With respect to the $15.0 million of cash received upon issuance of the shares, the Company applied equity accounting guidance to measure the $9.1 million recorded in equity upon the issuance of the shares, and the remaining $5.9 million was included as a component of the transaction price attributable to the revenue arrangement.

Accounting Analysis

The Company concluded that Alexion is a customer in this arrangement, and as such, the element of the arrangement unrelated to the issuance of the shares falls within the scope of the revenue recognition guidance. The Company identified the following promises under the arrangement: (i) the grant of licenses of intellectual property and know-how rights; (ii) the option to select additional targets; (iii) the option to perform validation testing on additional targets; (iv) associated research and development services for the initial and, as applicable, additional targets; and (v) participation in the joint steering committee. The Company concluded that the research and development services were not capable of being distinct from the research and development licenses, and were not distinct within the context of the contract, and should therefore be combined into a single performance obligation for each program. The Company considered the level of Alexion's therapeutic expertise specifically related to RNAi, as well as Alexion's know-how of the Company's GalXC conjugates, and concluded that Alexion cannot benefit from the granted license on its own or together with other resources that are readily available to Alexion, including relationships with oligonucleotide vendors who synthesize GalXC conjugates under contract with the Company. The Company also concluded that, while participation on the joint steering committee was capable of being distinct, participation is not distinct from the research and development services within the context of the contract, as they are both inputs to the combined output of a target that successfully achieves IND approval. As a result, the combination of the license of intellectual property together with the provision of research and development services and participation on the joint steering committee together represent the highest level of goods and services that can be deemed distinct.

Additionally, the Company determined that the options to select additional targets and to perform validation testing on additional targets were not priced at a discount and, as such, do not provide Alexion with material rights. Based on management's assessments, the Company identified a single performance obligation, namely, the combined license and research and development services, for each of the two initially nominated targets.

The Alexion Collaboration Agreement transaction price is $51.1 million, consisting of the $22.0 million upfront payment, the $5.9 million equity premium identified upon issuance of the shares, as described above, $19.5 million in aggregate contingent milestone payments that were either received or probable of achievement and under the Company's control, and $3.7 million of variable consideration for certain manufacturing initiatives reimbursed by Alexion.

The Company used the most likely amount method to estimate variable consideration and estimated that the most likely amount for each potential future development milestone payment under this agreement was zero, as the achievement of those milestones is uncertain and highly susceptible to factors outside of the Company's control. Accordingly, such milestones were initially excluded from the transaction price. Management reevaluates the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur and adjusts the transaction price as necessary. Sales-based royalties, including milestone payments based on the level of sales, were also excluded from the transaction price, as the license is deemed to be the predominant item to which the royalties relate. The Company will recognize such revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

Revenue associated with the performance obligation is being recognized as services are provided using an input method based on a cost-to-cost measure of progress. The transfer of control occurs over time and, in management's judgment, this input method is the

best measure of progress towards satisfying the performance obligations and reflects a faithful depiction of the transfer of goods and services.

In November 2019, the Company and Alexion amended the Alexion Collaboration Agreement (the "Alexion Amendment") to clarify funding of certain manufacturing costs for each of the two initial targets and increased milestone payments for the additional targets if Alexion exercised its options for the two additional targets.

In December 2019, Alexion exercised its options for the exclusive rights to two additional targets within the complement pathway for the discovery and development of GalXC molecules. These exercises expanded the companies' existing research collaboration and license agreement to now encompass four targets within the complement pathway. In connection with the option exercises, Alexion paid Dicerna a total of $20.0 million, or $10.0 million in option exercise fees per additional new target, that are being recognized into revenue as the related services are performed.

The Company concluded that the Alexion Amendment modified the original agreement, as the transaction price was changed as a result of Dicerna assuming responsibility for certain manufacturing costs associated with the initial targets. For accounting purposes, the exercise of the options created a separate new arrangement from the Alexion Collaboration Agreement for the two new targets.

The Company concluded that Alexion is a customer in the Alexion Amendment. The Company identified the following promises under the Alexion Amendment: (i) the grant of licenses of intellectual property and know-how rights, and (ii) associated research and development services for the additional targets. The Company concluded that the research and development services were not capable of being distinct from the licenses and were not distinct within the context of the contract, and should therefore be combined into a single performance obligation for each program. Similar to the initial targets, the Company considered the level of Alexion's therapeutic expertise specifically related to RNAi, as well as Alexion's know-how of the Company's GalXC conjugates, and concluded that Alexion could not benefit from the granted license on its own or together with other resources that are readily available to Alexion. As a result, the combination of the license of intellectual property together with the provision of research and development services represents the highest level of goods and services that can be deemed distinct. Based on management's assessments, the Company identified a single performance obligation, namely, the combined license and research and development services, for each of the two additional targets. The transaction price of the Alexion Amendment was determined to be $35.0 million, consisting of the $20.0 million in option exercise fees and $15.0 million in aggregate contingent milestone payments that were probable of achievement and under the Company's control.

The aggregate amount of the transaction price allocated to the Company's unsatisfied or partially unsatisfied performance obligations under the Alexion Agreements at June 30, 2021 was $39.2 million. As of June 30, 2021, the Company expects the majority of deferred revenue to be recognized through the third quarter of 2023.

The following table provides a summary of revenue recognized for the Alexion Agreement and the Alexion Amendment:

	THREE MONTHS ENDED JUNE 30,		SIX MONTHS ENDED JUNE 30,	
	2021	2020	2021	2020
Alexion Agreement	$ 2,316	$ 5,792	9,505	$ 7,914
Alexion Amendment	171	1,271	799	1,911
Total	$ 2,487	$ 7,063	$ 10,304	$ 9,825

The following tables provide a summary of deferred revenue balances for the Alexion Agreement and the Alexion Amendment:

	JUNE 30, 2021		
	CURRENT	NONCURRENT	TOTAL
Alexion Agreement	$ 6,951	$ 3,166	$ 10,117
Alexion Amendment	1,303	27,736	29,039
Total	$ 8,254	$ 30,902	$ 39,156

	DECEMBER 31, 2020		
	CURRENT	NONCURRENT	TOTAL
Alexion Agreement	$ 9,216	$ 7,528	$ 16,744
Alexion Amendment	9,464	20,323	29,787
Total	$ 18,680	$ 27,851	$ 46,531

BI agreement and related amendment

BI agreement – Background

On October 27, 2017, the Company entered into a collaborative research and license agreement with BI (the "BI Agreement"), pursuant to which the Company and BI jointly research and develop product candidates for the treatment of chronic liver disease using GalXC. 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 (the "Second Target"). Pursuant to the BI Agreement, Dicerna granted BI a worldwide license in connection with the research and development of such product candidates and transferred certain intellectual property rights of the selected product candidates to BI for clinical development and commercialization. Dicerna also may provide assistance to BI to help BI further develop selected product candidates. BI paid Dicerna a non-refundable upfront payment of $10.0 million for the first target. BI also agreed to reimburse Dicerna certain third-party expenses of $0.3 million.

Under the BI Agreement, the Company would have been eligible to receive potential development and commercial milestones as well as royalty payments on potential global net sales, subject to certain adjustments related to the first target, had BI determined to continue development of that target. BI's Second Target option provided for an option fee payment of $5.0 million and success-based development and commercialization milestones and royalty payments to Dicerna.

BI agreement – Accounting Analysis

The Company concluded that BI is a customer in this arrangement, and as such, the arrangement falls within the scope of the revenue recognition guidance. The Company identified the following promises under the contract: the license of intellectual property and conducting agreed-upon research program services. The Company concluded that the license and research and development services are not capable of being distinct and are not distinct within the context of the contract; therefore, the Company considers these to be one performance obligation. The Company concluded that the option underlying the transfer of future licenses and potential associated research for any not-yet-known target gene is not a performance obligation of the contract at inception because the option fee reflects the standalone selling price of the option, and therefore, the option is not considered to be a material right. The Company considered the level of BI's therapeutic expertise specifically related to RNAi, as well as BI's know-how with regard to the Company's GalXC conjugates, and concluded that BI cannot benefit from the granted license on its own or together with other resources that are readily available to BI, including relationships with oligonucleotide vendors who synthesize GalXC conjugates under contract with the Company. As a result, the combination of the license of intellectual property together with the provision of research and development support services represents the highest level of goods and services that can be deemed distinct.

Based on management's evaluation, the $10.0 million non-refundable upfront fee and the $0.3 million agreed-upon reimbursable third-party expenses constituted the amount of the consideration to be included in the transaction price and were allocated to the performance obligation identified. None of the development milestones were included in the transaction price during the period, since none of such milestone amounts were within the control of the Company and were not considered probable to occur until confirmed by BI, at BI's sole discretion. Any consideration related to commercial sales-based milestones related to the first target (including royalties) would have been recognized at the later of (i) when the related sales occurred, or (ii) when the performance obligation to which some or all of the royalty had been allocated had been satisfied (or partially satisfied).

The $10.3 million transaction price for the first target was recognized through July 2019, which was the point when the Company's obligation to provide research support services to BI for the first target ended. Related revenue was recognized on a straight-line basis, which was, in management's judgment, an appropriate measure of progress toward satisfying the performance obligation.

BI agreement-related amendment – Background

In October 2018, BI exercised its Second Target option, which entitled the Company to a non-refundable payment of $5.0 million and reimbursement of $0.7 million for certain third-party expenses. The terms of the Second Target option exercise and related rights and obligations associated with the Second Target were agreed to in an Additional Target Agreement (the "ATA"), as amended, which was entered into on December 31, 2018.

Under the terms of the ATA, BI is responsible for future clinical development and commercialization of candidate products for the Second Target. Additionally, during the term of the research program, BI will reimburse the Company for certain expenses. The Company is eligible to receive up to $170.0 million in potential development and commercial milestones related to the Second Target. The Company is also eligible to receive tiered royalty payments on potential global net sales, subject to certain adjustments, in the mid-single digits. Except as otherwise set forth in the ATA, development of the Second Target is subject to the terms of the original BI Agreement.

BI agreement-related amendment – Accounting Analysis

The exercise of the Second Target option on December 31, 2018 through the ATA created a new arrangement for accounting purposes, and management determined that the $5.0 million exercise price with the $0.7 million of reimbursable expenses was representative of the standalone selling price. Consistent with the reasons described related to the first target, management concluded that the non-refundable Second Target option exercise fee (akin to an upfront payment) and reimbursable expenses constituted the amount of the consideration to be included in the transaction price and were allocated to the single performance obligation. The basis for the conclusions regarding the treatment of development and sales-based milestones associated with the Second Target are consistent with those associated with the initial combined performance obligation under the BI Agreement. Management reevaluates the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

Consistent with the first target, revenue is recognized on a straight-line basis, which is in management's judgment an appropriate measure of progress toward satisfying the performance obligation. The Company began recognizing the $5.7 million transaction price as revenue in January 2019 and continued through November 2020, which was the point when the Company's obligation to provide research support services to BI for the Second Target ended. In May 2021, the Company announced that BI had accepted a GalXC RNAi candidate for advancement under the ATA. Acceptance of the DCR-LIV2 compound as a development candidate triggered a single-digit multimillion-dollar milestone payment to Dicerna, which the Company received and recognized in full in the second quarter of 2021. There were no unsatisfied performance obligations under the BI ATA at June 30, 2021.

In addition to establishing the terms of the Second Target option exercise, the ATA also amended the BI Agreement to provide the parties the opportunity to consider the development of product candidates targeting a further additional target gene (the "Third Target Option"). Per the ATA, if BI elects to exercise the Third Target Option following Dicerna's presentation of data for a new product candidate, the parties must also agree to a research work plan and budget for the additional gene and negotiate development and commercialization milestones and royalty payments to the Company, and upon such agreement and consummation of such exercise, BI would make an option fee payment to the Company of $5.0 million. This option exercise fee is consistent with the Second Target option exercise fee, which management concluded was representative of the standalone selling price. If BI chooses to exercise the Third Target Option, the Company will be responsible for the discovery and initial profiling of the product candidates, including primary preclinical studies, synthesis, and delivery. BI will be 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 preclinical development, clinical development, manufacturing, and commercialization of those products. If the Third Target Option is exercised, such exercise would result in a new arrangement for accounting purposes, as the licensing rights and research and development services underlying the Third Target Option are distinct from those associated with the first and Second Targets.

Revenue summary

The following table provides a summary of revenue recognized:

	THREE MONTHS ENDED JUNE 30,		SIX MONTHS ENDED JUNE 30,	
	2021	2020	2021	2020
Novo	$ 6,700	$ 2,447	$ 13,312	$ 4,052
Roche	14,234	20,677	39,845	39,984
Lilly	14,735	9,487	22,298	19,069
Alexion	2,487	7,063	10,304	9,825
BI	3,181	774	3,181	1,546
Total	$ 41,337	$ 40,448	$ 88,940	$ 74,476

The following tables provide a summary of deferred revenue balances:

	JUNE 30, 2021		
	CURRENT	NONCURRENT	TOTAL
Novo	$ 36,829	$ 142,795	$ 179,624
Roche	62,022	55,019	117,041
Lilly	53,095	39,890	92,985
Alexion	8,254	30,902	39,156
Total	$ 160,200	$ 268,606	$ 428,806

	DECEMBER 31, 2020		
	CURRENT	NONCURRENT	TOTAL
Novo	$ 30,169	$ 162,630	$ 192,799
Roche	49,493	81,273	130,766
Lilly	40,195	64,482	104,677
Alexion	18,680	27,851	46,531
Total	$ 138,537	$ 336,236	$ 474,773

The Company recognized the following revenues as a result of changes in contract liability balances:

	THREE MONTHS ENDED JUNE 30,		SIX MONTHS ENDED JUNE 30,	
	2021	2020	2021	2020
Amounts included in deferred revenue at the beginning of the period [1]	$ 31,947	$ 38,595	$ 60,260	$ 65,278
Performance obligations satisfied (or partially satisfied) in previous reporting periods [2]	$ 6,431	$ 1,011	$ 20,188	$ 2,004

[1] The Company determines the revenue recognized in each period from contract liabilities by first attributing revenue to the individual contract liability balance outstanding at the beginning of the period. If additional consideration is received on those contracts in subsequent periods, we assume all revenue recognized in the reporting period first applies to the beginning contract liability as opposed to the new consideration for the period.

[2] Relates to changes in estimated costs for the Company's future performance obligations and estimated variable consideration

7. ROYALTY PHARMA FINANCING

Pursuant to the PH Agreement between Dicerna and Alnylam that was signed in 2020, Dicerna became entitled to royalties on worldwide net product sales of Alnylam's PH product, OXLUMO™ (lumasiran). Under the terms of the PH Agreement, Dicerna was entitled to royalties in the mid- to high-single-digits based on OXLUMO global net sales. Refer to Note 6 – Collaborative Research And License Agreements for further information.

In April 2021, the Company sold its right to receive royalties from sales of OXLUMO to Royalty Pharma plc for an upfront cash payment of $180.0 million and up to $60.0 million in contingent sales-based milestone payments. The Company evaluated the arrangement to determine whether the upfront payment should be accounted for as debt or deferred income and determined that, as none of the criteria for classification as debt had been met, the proceeds from the upfront payment should be recorded as deferred income on the condensed consolidated balance sheets. The Company applies the "units-of-revenue" method of recognition of this income in the condensed consolidated statements of operations, and such amounts are recorded in other (expense) income.

8. STOCK-BASED COMPENSATION

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

	THREE MONTHS ENDED JUNE 30,		SIX MONTHS ENDED JUNE 30,	
	2021	2020	2021	2020
Research and development expenses	$ 7,143	$ 4,578	$ 13,577	$ 8,881
General and administrative expenses	6,490	5,628	12,469	9,852
Total	$ 13,633	$ 10,206	$ 26,046	$ 18,733

During the three and six months ended June 30, 2021, the Company granted stock options to purchase 285,375 and 2,254,022 shares of common stock with aggregate grant date fair values of $5.6 million and $37.4 million, respectively, compared to stock options to purchase 701,925 and 3,608,225 shares of common stock granted with aggregate grant date fair values of $9.5 million and $53.8 million during the three and six months ended June 30, 2020, respectively.

The assumptions used to estimate the grant date fair value using the Black-Scholes option pricing model were as follows:

	THREE MONTHS ENDED JUNE 30,		SIX MONTHS ENDED JUNE 30,	
	2021	2020	2021	2020
Common stock price	$25.76 - $30.71	$17.33 - $21.61	$22.07 - $30.71	$15.61 - $22.58
Expected option term (in years)	5.27 - 6.08	5.50 - 6.08	5.27 - 6.08	5.50 - 6.08
Expected volatility	77.72% - 79.16%	78.33% - 80.45%	77.72% - 79.16%	78.33% - 80.45%
Risk-free interest rate	0.90% - 1.15%	—% - 0.42%	0.51% - 1.15%	—% - 1.71%
Expected dividend yield	—%	—%	—%	—%

During the three and six months ended June 30, 2021, the Company granted 63,489 and 502,799 restricted stock units with grant date fair values of $1.9 million and $12.4 million, respectively, compared to 189,455 and 910,055 restricted stock units with grant date fair values of $3.8 million and $19.8 million during the three and six months ended June 30, 2020, respectively.

9. INCOME TAXES

During the three months ended June 30, 2021, the Company recorded an income tax provision of $0.5 million, resulting in an effective tax rate of approximately 0.79% for the six months ended June 30, 2021. The difference between the effective tax rate and the federal statutory tax rate primarily relates to changes in the valuation allowance on net deferred tax assets. The tax expense largely relates to federal tax payable that is not expected to be fully offset by any tax attributes.

10. LEASES

On January 14, 2020, the Company entered into a non-cancelable real property lease agreement for 61,282 square feet of laboratory and office space at 75 Hayden Avenue in Lexington, Massachusetts (the "75 Hayden Avenue" lease). The original term commenced during the fourth quarter of 2020 and is for 125 months with options to extend for two additional successive periods of five years thereafter. On July 1, 2020, the Company entered into an amendment to the 75 Hayden Avenue lease (the "75 Hayden Amendment"). The 75 Hayden Amendment expanded the square footage leased under the 75 Hayden Avenue lease by 30,446 square feet to contain a total of 91,728 rentable square feet and increased the monthly base rent by an average of $0.2 million per month.

The term for the additional space under the 75 Hayden Amendment commenced for accounting purposes during the second quarter of 2021 and is for 118.5 months with options to extend for two additional successive periods of five years thereafter. Payments for the extensions are not included in measurement of the right-of-use ("ROU") asset and lease liability, as it is not reasonably certain that the Company will exercise its options to extend the lease term. The aggregate total fixed rent for the 75 Hayden Amendment is approximately $21.3 million with the annual fixed rental payments increasing from $1.9 million to $2.6 million during the amended

term. The Company recognized an ROU asset and a lease liability of approximately $17.2 million and $15.3 million, respectively, in the three months ended June 30, 2021 related to the 75 Hayden Amendment.

The interest rate implicit in the lease agreement is not readily determinable, and as such, the Company utilizes its incremental borrowing rate to calculate the lease liability, which is the rate incurred to borrow, on a collateralized basis for a similar term, an amount equal to the lease payments in a similar economic environment at the time the asset is made available to the Company.

11. COMMITMENTS AND CONTINGENCIES

From time to time, the Company may be subject to various claims and legal proceedings in the ordinary course of business. If the potential loss from any claim, asserted or unasserted, or legal proceeding is considered probable and the amount is reasonably estimable, the Company will accrue a liability for the estimated loss. There were no contingent liabilities recorded as of June 30, 2021.

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those discussed here. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in this section as well as factors described in Part II, Item 1A – "Risk Factors" and "Special Note Regarding Forward-Looking Statements" included elsewhere in this Quarterly Report on Form 10-Q.

Overview

Dicerna Pharmaceuticals, Inc. ("we," "us," "our," "the Company," or "Dicerna") is a biopharmaceutical company focused on discovering, developing, and commercializing medicines that are designed to leverage ribonucleic acid interference ("RNAi") to silence selectively genes that cause or contribute to disease. Using our proprietary GalXC™ and GalXC-Plus™ RNAi technologies, Dicerna is committed to developing RNAi-based therapies with the potential to treat both rare and more prevalent diseases. By silencing disease-causing genes, Dicerna's GalXC platform has the potential to address conditions that are difficult to treat with other modalities. Initially focused on disease-causing genes in the liver, Dicerna has continued to innovate and is exploring new applications of its RNAi technology with GalXC-Plus, which expands the functionality and application of our flagship liver-based GalXC technology to tissues and cell types outside the liver and has the potential to treat diseases across multiple therapeutic areas. In addition to our own pipeline of core discovery and clinical candidates, Dicerna has established collaborative relationships with some of the world's leading pharmaceutical companies, including Novo Nordisk A/S ("Novo"), Roche, Eli Lilly and Company ("Lilly"), Alexion Pharmaceuticals, Inc. (together with its affiliates, "Alexion"), Boehringer Ingelheim International GmbH ("BI"), and Alnylam Pharmaceuticals, Inc. ("Alnylam"). Between Dicerna and our collaborative partners, we currently have more than 20 active discovery, preclinical, or clinical programs focused on cardiometabolic, viral, chronic liver, and complement-mediated diseases, as well as neurodegenerative diseases and pain.

Most of our drug discovery and development efforts are based on the therapeutic modality of RNAi, a highly potent, natural, and specific mechanism that can be directed to reduce expression of a target gene. In this naturally occurring biological process, a short, synthetic, double-stranded RNA duplex induces the enzymatic destruction of the messenger ribonucleic acid ("mRNA") of a target gene that contains sequences complementary to one strand of a double-stranded RNA. Our approach is to design proprietary RNA molecules that have the potential to engage the enzyme Dicer and direct the endogenous cellular RNAi machinery to silence a specific therapeutic target gene. Our GalXC technology utilizes a proprietary GalNAc-mediated conjugate to cause the liver to efficiently internalize our synthetic RNA molecules. In contrast, our GalXC-Plus technology incorporates new chemistries and secondary structures designed to enable the targeting of genes in tissues and cell types beyond the liver. Our current clinical programs utilize the GalXC technology. Our GalXC-Plus technology utilizes modified RNA structures and various fully synthetic conjugated ligands for delivery to non-liver tissues and is used in a number of our preclinical programs. Due to the enzymatic nature of RNAi, a single GalXC or GalXC-Plus molecule incorporated into the RNAi machinery can destroy hundreds or thousands of mRNAs from the targeted gene.

The GalXC RNAi platform and other proprietary RNAi delivery technologies support Dicerna's long-term strategy to retain a full or substantial ownership stake in our programs, subject to the evaluation of potential licensing opportunities as they may arise, and to invest internally in programs for diseases with focused patient populations, such as certain rare diseases or diseases with well-characterized genetic targets. These certain rare disease programs represent opportunities that we believe may carry a relatively higher probability of success, with genetically and molecularly defined disease markers, high unmet medical need, a limited number of centers of excellence to facilitate reaching these patients, and/or the potential for more rapid clinical development paths to regulatory approval. For more complex diseases with multiple gene dysfunctions and/or larger patient populations, we continue to pursue collaborations that can provide the enhanced scale, resources, and commercial infrastructure required to maximize these prospects.

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

Executive Summary

The following table provides a summary of revenue recognized for the three and six months ended June 30, 2021 (amounts in thousands):

	THREE MONTHS ENDED JUNE 30, 2021	SIX MONTHS ENDED JUNE 30, 2021
Novo	$ 6,700	$ 13,312
Roche	14,234	39,845
Lilly	14,735	22,298
Alexion	2,487	10,304
BI	3,181	3,181
Total	$ 41,337	$ 88,940

Payments received from our collaboration partners during the three and six months ended June 30, 2021 were as follows (amounts in thousands):

	THREE MONTHS ENDED JUNE 30, 2021	SIX MONTHS ENDED JUNE 30, 2021
Novo	$ 107	27,607
Roche	26,102	27,852
Lilly	10,094	10,779
Alexion	2,798	5,209
BI	2,525	3,092
Total	$ 41,626	$ 74,539

Our results of operations for and liquidity and capital resources as of the six months ended June 30, 2021 include the following:

- In February 2021, Lilly notified us of their decision to extend for an additional year the initial research collaboration term for the extrahepatic targets subject to our collaboration and license agreement with Lilly (the "Lilly Collaboration Agreement"). Under the Lilly Collaboration Agreement, Lilly has the option to extend the three-year initial research collaboration term for these extrahepatic targets for up to three consecutive one-year periods. This first extension allows the research program for these extrahepatic targets under the Lilly Collaboration Agreement to continue through October 2022.
- In March 2021, Roche initiated RG6346 in a Roche-sponsored Phase 2 combination trial for the treatment of chronic hepatitis B ("HBV") infection, which entitled us to a $25.0 million milestone payment under our collaboration and license agreement with Roche (the "Roche Collaboration Agreement"). We received this payment in the second quarter of 2021.
- In April 2021, we announced that Royalty Pharma plc ("Royalty Pharma") had acquired our royalty interest in Alnylam's OXLUMO (lumasiran) for an upfront cash payment of $180.0 million and up to $60.0 million in contingent sales-based milestone payments.
- In May 2021, we announced that BI had accepted a GalXC RNAi candidate for advancement under the collaborative research and license agreement with BI (the "BI Agreement") as amended and supplemented by the Additional Target Agreement (the "ATA"). Acceptance of the DCR-LIV2 compound as a development candidate triggered a single-digit multimillion-dollar milestone payment to Dicerna, which we received and recognized in full in the second quarter of 2021.
- In May 2021, the U.S. Food and Drug Administration ("FDA") accepted the Investigational New Drug ("IND") application filed by Lilly for LY3819469, targeting the *LPA* gene as a potential treatment for cardiometabolic diseases, triggering a $10.0 million payment to Dicerna under the Lilly Collaboration Agreement. We received this payment in the second quarter of 2021.
- We believe we have sufficient capital, along with anticipated milestone and other payments from existing collaborations, to fund the execution of our current clinical and operating plans into 2025.

COVID-19 Update

On March 11, 2020, the World Health Organization declared the spread of COVID-19 a pandemic. The global spread of COVID-19 has created significant volatility, uncertainty, and economic disruption worldwide. Governments in affected regions have

implemented, and may continue to implement, safety precautions which include quarantines, travel restrictions, business closures, and other public health safety measures.

Throughout 2020 and into 2021, we were impacted by mandatory work from home edicts directed by local governments in the jurisdictions in which we operate. However, essential work exemptions continued to permit critical research and development and laboratory activities for limited personnel. Those exemptions enabled some continued discovery research and activities supporting our collaborative agreements and our own programs. Externally, the COVID-19 pandemic has resulted in some challenges in reserving slots for preclinical studies and accessing non-human primates for such studies, as well as slower enrollment in our clinical trials. We have undertaken efforts to mitigate potential impacts to our business including those related to conducting clinical trials and managing our supply chain. Our operating results could be affected by delays or suspensions of clinical development associated with COVID-19, which have impacted and may continue to impact global healthcare systems and our trial sites' enrollment in our clinical trials, such as we have seen in the nedosiran and belcesiran studies, and delays in the supply chain related to COVID-19. We continue to be alert to the potential for disruptions that could arise from COVID-19 or its variants and monitor the FDA's and other health authorities' guidance for the conduct of clinical trials during this time.

We conduct clinical trials in various countries around the world, including the United States ("U.S") and other areas heavily impacted by the COVID-19 pandemic. The current supply of our investigational medicines is sufficient to support ongoing and planned clinical trials. Based on current evaluations, our supply chain continues to appear intact to meet at least the next 18 months of clinical, nonclinical, commercial, and chemistry, manufacturing, and control ("CMC") supply demands across all programs. We have undertaken efforts to mitigate potential future impacts to the supply chain by increasing our stock of critical starting materials required to meet our needs and our collaborative partners' needs through 2022 and by identifying and engaging alternative suppliers. We continue to be alert to the potential for disruptions that could arise from COVID-19 or its variants and remain in close contact with suppliers.

It is difficult to predict what the lasting impact of the pandemic will be, and what the impact might be if we or any of the third parties with whom we engage were to experience additional shutdowns or other prolonged business disruptions. Our ability to conduct our business in the manner and on the timelines presently planned could have a material adverse impact on our business, results of operations, and financial condition. In addition, depending on the duration and impact of the recurrence or resurgence of COVID-19 cases or continued evolution of further strains of COVID-19 or its variants, and depending on where the infection rates are highest, and including the ability of regulators to continue ensuring the timely review and approval of applications, our business, results of operations, and financial condition may be negatively impacted. We will continue to monitor developments as we deal with the disruptions and uncertainties relating to the COVID-19 pandemic. Please refer to the "Financial Operations Overview" section below for specific anticipated effects on our financial statement line items.

Our GalXC Platform

The GalXC RNAi Platform

Dicerna's GalXC platform consists of our liver-targeted GalXC technology and our GalXC-Plus technology for tissues outside the liver. Each utilizes a set of proprietary double-stranded RNA structures capable of inducing RNAi and associated chemical modifications and additions to these structures that enhance their properties and help confer useful "drug-like" properties. Our RNAi-inducing RNA structures consist of two strands of RNA. One of these strands, called the guide strand, is complementary to the mRNA sequence of the gene one is seeking to inhibit. The other strand, called the passenger strand, includes sequences complementary to the guide strand, forming a double-stranded RNA duplex with it. In the case of our GalXC and GalXC-Plus technologies, additional sequences may be added to the passenger strand, including a four-base sequence, known as a tetraloop, which is designed to enhance stability and engineer out immunostimulatory activity and can serve as an attachment point for various chemical additions that can facilitate delivery to diverse tissues.

GalXC RNAi Technology Targeted to the Liver

To target the liver, we conjugate the tetraloop region of our GalXC molecules to a simple natural sugar, GalNAc, that is specifically recognized by a receptor on the surface of liver hepatocytes. This leads to internalization, ultimately enabling the GalXC molecules to access the RNAi machinery inside the hepatocyte and deliver our targeted oligonucleotide to the RNA-induced silencing complex ("RISC"). Due to the efficiency of this process, a full human dose may be administered via a single subcutaneous injection.

GalXC-Plus RNAi Technology for Tissues Outside the Liver

For delivering to tissues outside the liver and/or cell types other than hepatocytes, we have continued to innovate our GalXC platform using modified structures, chemistries, and conjugated delivery moieties. Referred to as GalXC-Plus, these proprietary technological advances extend our expertise in RNAi silencing to address new tissues and organs outside the liver and to non-hepatocyte cells in the liver, while retaining key pharmacological features from GalXC.

Development Approach

In choosing which development programs to internally advance, we apply the scientific, clinical, and commercial criteria that we believe allow us to best leverage our GalXC and GalXC-Plus RNAi technologies and maximize value. Using our GalXC RNAi technology, and applying the criteria of our development focus, we have created a pipeline of core liver-targeted therapeutic programs for development by Dicerna. For opportunities that were not selected as core program opportunities, we have sought partners to fund the discovery, and subsequently drive the development of, these non-core opportunities in exchange for upfront payments, milestone payments, royalties on product sales, and potentially other economic and operational arrangements. Our current collaborations with Novo, Lilly, Alexion, and BI resulted from this effort. For core programs targeting rare diseases, we intend to develop these programs internally through approval. For core programs targeting larger populations, we may seek development partners, such as our collaboration with Roche on RG6346, under various economic and operational arrangements. Together, our core program pipeline and our pipeline of non-core collaborative programs constitute a broad and growing therapeutic pipeline that we believe may result in multiple valuable approved products based on our GalXC and GalXC-Plus technologies.

In addition to the programs listed in our pipeline, we are exploring a variety of potential programs involving gene targets in diverse tissues addressable with our GalXC and GalXC-Plus technologies. Some of these programs may be elevated in the future to be either a core program or a non-core collaborative program. Under our collaborations with Novo, Roche, and Lilly, our collaborators have rights to nominate additional programs for discovery by Dicerna and subsequent development by the nominating collaborator, which will become part of our collaborative pipeline. In the case of our collaboration with Novo, we retain rights to opt in to deeper participation, including enhanced economic rights, at defined points in clinical development, for two programs nominated by Novo.

Our four current core GalXC development programs are: nedosiran for the treatment of primary hyperoxaluria (“PH”), RG6346 for the treatment of chronic HBV infection, belcesiran (formerly DCR-A1AT) for the treatment of alpha-1 antitrypsin deficiency-associated liver disease (“AATLD”), and DCR-AUD for the treatment of alcohol use disorder (“AUD”).

We conduct clinical trials in various countries around the world, including the U.S. and other areas heavily impacted by the COVID-19 pandemic. The current supply of our investigational medicines is sufficient to support ongoing and planned clinical trials. Based on current evaluations, our supply chain continues to appear intact to meet at least the next 18 months of clinical, nonclinical, commercial, and CMC supply demands across all programs. We have undertaken efforts to mitigate potential future impacts to the supply chain by increasing our stock of critical starting materials required to meet our needs and our collaborative partners’ needs through 2022 and by identifying and engaging alternative suppliers. In 2020, there were delays related to several nedosiran PHYOX programs and the belcesiran clinical trial in healthy volunteers as a result of COVID-19. As a result, and based on the most recent updates from clinical sites impacted by COVID-19 and precautionary measures related to the pandemic, we regularly evaluate our expectations related to clinical development milestones.

The table below sets forth the stages of development of our various GalXC RNAi platform product candidates as of August 9, 2021:

TARGET INDICATION	COMPOUND (GENE TARGET)	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	DICERNA PRODUCT RIGHTS	PARTNER
Primary Hyperoxaluria 1, 2 & 3	Nedosiran (*LDHA*)					100% global	
Chronic Hepatitis B	RG6346 (*HBV*)					U.S. opt-in	Roche
AAT Liver Disease	Belcesiran (*SERPINA1*)					100% U.S. (Alnylam ex-U.S. opt-in)	Alnylam
Alcohol Use Disorder	DCR-AUD (*ALDH2*)					100% global	
Cardiometabolic	LY3561774 (*ANGPTL3*)					Milestone/royalty	Lilly
Cardiometabolic	LY3819469 (*LPA*)					Milestone/royalty	Lilly
Cardiometabolic	DCR-CM4					Milestone/royalty	Lilly
Cardiometabolic	DCR-CM3					Milestone/royalty	Lilly
Complement-mediated	DCR-COMP1 (*C3*)					Milestone/royalty	Alexion
Complement-mediated	DCR-COMP2 (*CFB*)					Milestone/royalty	Alexion
Cardiometabolic	DCR-NOVO1					Opt-in to co-dev. and co-comm.	novo nordisk
Cardiometabolic	DCR-NOVO2					Opt-in to co-dev. and co-comm.	novo nordisk
Nonalcoholic Steatohepatitis	DCR-LIV2					Milestone/royalty	Boehringer Ingelheim
Undisclosed GalXC-Plus						100% global	
Undisclosed GalXC-Plus						100% global	

Anticipated Timing: *IND/CTA filings for DCR-CM4 and DCR-CM3 are the responsibility of Lilly and are at their discretion. Dicerna estimates IND timing for DCR-CM4 in Q1’22.*
Dicerna intends to deliver IND-supporting packages to Alexion for DCR-COMP1 and DCR-COMP2 in Q4’21 and Q1’22, respectively; IND/CTA filings are the responsibility of Alexion and are at their discretion.

Research

We continue to advance our GalXC RNAi platform as it is applied to therapeutic targets expressed in hepatocytes using GalNAc conjugates for both our collaborative research and development programs and our internal liver-targeted programs. All current Dicerna collaborations include one or more liver-targeted applications of the GalXC RNAi technology.

In addition, we are exploring applications of our GalXC-Plus RNAi technology against therapeutic gene targets expressed in tissues other than the liver, including targets expressed in the central nervous system ("CNS"), muscle tissue, adipose tissue, tumor-associated immune cells, and other tissues. We have achieved significant gene target knockdown (i.e., reduction in the expression of target mRNA activity and disease biomarker activity) in multiple cell types and regions of the CNS and other extrahepatic tissues, in both rodents and non-human primates ("NHPs"). These extrahepatic applications are based on proprietary modifications to our well-characterized, clinical-stage GalXC platform that enable extrahepatic delivery and pharmacological activity.

In August 2020, we first presented preclinical data related to our GalXC-Plus RNAi technology in the CNS, skeletal muscle, and adipose tissues. Results from preclinical studies demonstrated consistent and durable CNS-wide target mRNA knockdown using novel constructs regardless of route of administration (intrathecal [IT] or intracisterna magna [ICM]), and reduction in target mRNA in skeletal muscle and adipose tissue using optimized chemistries, resulting in equivalent and potentially highly durable target knockdown regardless of dosing regimens.

In March 2021, we presented new preclinical data related to our GalXC-Plus technology demonstrating its potential to deliver deep and sustained mRNA knockdown against prespecified gene targets across the CNS and to specific CNS cell types. Data from a preclinical mouse study showed that a single dose of an unconjugated GalXC-Plus molecule engineered to silence mRNA produced by the *ALDH2* gene, a widely occurring and common genetic test target, resulted in dose-dependent reductions of up to 92% knockdown in target mRNA across the CNS that lasted through the trial conclusion at 28 days. GalXC-Plus delivered similar mRNA reductions in NHP studies after a single dose, resulting in up to 90% target mRNA silencing after 28 days. There were no adverse observations for any GalXC-Plus cohort in these trials. Additional preclinical data demonstrated the degree and distribution of GalXC-Plus silencing of β-tubulin III (*Tubb3* gene; expressed in neurons and associated with various cancers) and two undisclosed gene targets expressed by astrocytes and oligodendrocytes, respectively, using unconjugated and various conjugated GalXC-Plus payloads:

- **Oligodendrocytes**: There was a clear reduction of target mRNA in oligodendrocytes across the brain and spinal cord of rodents following a single, lumbar intrathecal or intracisternal GalXC-Plus dose with up to 80% target mRNA silencing after seven days. In NHPs, there was a clear dose-related relationship between GalXC-Plus intracisternal administration and target mRNA reduction with up to 85% target mRNA reduction maintained for approximately three months. There were no adverse observations for any GalXC-Plus cohort in these trials.
- **Astrocytes**: GalXC-Plus demonstrated a clear reduction in target mRNA in mouse astrocytes after a single lumbar intrathecal injection. An ongoing preclinical study also shows durable control of target mRNA expression, with up to 80% target mRNA reduction maintained for at least 160 days. The durability in rodents was independent of the initial magnitude of target knockdown.
- **Neurons**: The flexibility of the GalXC-Plus technology enabled additional conjugations to optimize delivery to neuronal cells, resulting in clear, CNS-wide reductions (up to 95%) in neuronal-specific Tubb3 mRNA after a single lumbar intrathecal dose in mice. Comparisons of target knockdown potency across astrocyte and neuronal cells using multiple GalXC-Plus conjugate modifications indicated the potential for complementary and tunable knockdown across multiple CNS cell types.

Status of Dicerna Programs

Our current core GalXC RNAi platform development programs are as follows:

Nedosiran for Primary Hyperoxaluria

Nedosiran is the only RNAi drug candidate in development for the treatment of PH type 1 ("PH1"), PH type 2 ("PH2"), and PH type 3 ("PH3") and is our most advanced product candidate utilizing the proprietary GalXC RNAi technology platform. PH is a family of ultra-rare, life-threatening genetic disorders that initially manifest with complications in the kidneys. These genetic mutations cause enzyme deficiencies that result in the overproduction of a substrate called oxalate. Abnormal production and accumulation of oxalate leads to recurrent kidney stones, diffuse deposits of calcium oxalate in the kidneys (nephrocalcinosis), and chronic kidney disease that may progress to end-stage renal disease requiring intensive dialysis. Genetic studies suggest approximately 8,500 people in the U.S. are affected by PH, and researchers estimate that more than 80% of patients remain undiagnosed. There is currently only one approved therapy available specifically for the treatment of patients with PH1.

As PH is characterized by overproduction of oxalate in the liver, patients with PH are predisposed to the development of recurrent urinary tract (urolithiasis) and kidney (nephrolithiasis) stones, composed of calcium oxalate crystals formed from the excess

oxalate. Stone formation is accompanied by nephrocalcinosis of some patients with PH, which produces tubular toxicity, inflammation, and renal damage. This injury is compounded by the effects of renal calculi-related obstruction, frequent superimposed infections, and damage due to procedures needed to relieve stone-related obstruction. Compromised renal function eventually results in the accumulation of oxalate in a wide range of organs including the skin, bones, eyes, and heart. In the most severe cases, symptoms start in the first year of life. A combined liver-kidney transplant may be undertaken to resolve PH1 or PH2, but it is an invasive solution with limited availability and high morbidity that requires lifelong immune suppression to prevent organ rejection.

PH encompasses three genetically distinct, autosomal-recessive, inborn errors of glyoxylate metabolism characterized by the overproduction of oxalate. PH1, PH2, and PH3 are each characterized by a specific enzyme deficiency. PH1 is caused by a deficiency of glyoxylate-aminotransferase, PH2 is caused by a deficiency of glyoxylate reductase/hydroxypyruvate reductase, and PH3 is caused by a deficiency of 4-hydroxy-2-oxoglutarate aldolase. The last step in the production of oxalate in the liver involves the enzyme product of the *LDHA* gene. Our nedosiran product candidate seeks to block production of the lactate dehydrogenase enzyme by silencing the *LDHA* gene.

PHYOX™1 Single-Ascending-Dose Study

Data from the completed PHYOX1 trial, a Phase 1 single-ascending-dose study of nedosiran in healthy volunteers and study participants with PH1 or PH2, showed that nedosiran was generally well-tolerated in healthy volunteers and PH participants, and no serious safety concerns were identified in this study. In addition, nedosiran administration was associated with normalization or near-normalization of urinary oxalate (“Uox”) levels in 14 of 18 (78%) participants with PH1 or PH2 following a single dose. We define normal and near-normal (1.3x normal) Uox as below 0.46 mmol/1.73m^2 BSA/24 hr and from 0.46 to 0.6 mmol/1.73m^2 BSA/24 hr, respectively.

PHYOX2 Multidose, Double-Blind, Randomized, Placebo-Controlled Pivotal Trial

PHYOX2 is a Phase 2 multidose, double-blind, placebo-controlled pivotal trial designed to evaluate the efficacy, safety, and tolerability of nedosiran over six months in participants aged six years and older who have PH1 or PH2. This global trial includes countries across North America, Europe, and other regions, including Japan, Australia, and New Zealand. Participants were randomized 2:1 to a fixed monthly dose of nedosiran or placebo administered once monthly by subcutaneous injection. The primary endpoint of the study was the percent change from baseline in area under the curve of 24-hour Uox excretion between Days 90 and 180. The key secondary endpoint was percentage of PH1 and PH2 patients achieving normalization or near-normalization on at least two consecutive visits from Day 90 to Day 180. Enrollment in the PHYOX2 trial has been completed globally, and the last patient completed dosing in the second quarter of 2021.

In August 2021, we announced positive top-line results from the pivotal PHYOX2 clinical trial of nedosiran. Nedosiran achieved the primary endpoint in the PHYOX2 trial, demonstrating a statistically significant reduction from baseline in Uox excretion compared to placebo ($p<0.0001$). The study also achieved the key secondary endpoint, with a significantly higher proportion of patients administered nedosiran achieving and sustaining normal or near-normal Uox at two or more consecutive visits after Day 90 compared to placebo ($p=0.0025$). Uox reductions were significant in participants with PH1 while participants with PH2 (5 nedosiran and 1 placebo) showed inconsistent results in this trial. Nedosiran was generally well tolerated in the study with an overall adverse event profile consistent with previously reported data from PHYOX trials.

PHYOX3 Long-Term, Multidose, Open-Label Extension Study

Following positive Phase 1 data from PHYOX1 in 2019, we received clearance to proceed with the pivotal trial (PHYOX2) and PHYOX3, a long-term, multidose, open-label, extension study of nedosiran in PH. Unlike the PHYOX2 trial, which requires screening and enrollment of new participants, patients are permitted to transition into the PHYOX3 trial from any previous nedosiran trial in which they have participated and have completed.

The primary endpoint of PHYOX3 is to evaluate the impact of monthly nedosiran administration on the annual rate of decline in estimated glomerular filtration rate, a measure of kidney function. The PHYOX3 trial will also evaluate the long-term effect of nedosiran on Uox excretion, new stone formation, progression of nephrocalcinosis, and the potential to enable the gradual decrease or elimination of patients’ supportive hyperhydration therapies.

Additional PHYOX Trials: PHYOX4, PHYOX7, PHYOX8, and PHYOX-OBX

Given the fluid nature of the COVID-19 pandemic and the evolving and extraordinary actions undertaken by clinical trial sites globally, we continue to evaluate our clinical plans related to nedosiran. At this time, the status of additional PHYOX trials is as follows:

- PHYOX4: Enrollment in a study of patients with PH3 began in January 2021 and the first patient was dosed in February 2021. We completed dosing in June 2021 and anticipate reporting top-line results from the study in October 2021.
- PHYOX7: Enrollment in a study of patients with PH1 or PH2 and severe renal impairment, including those on dialysis, began in the first quarter of 2021 and patient dosing is underway.
- PHYOX8: An open-label study of patients with PH1 or PH2 aged 0-5 years with relatively intact renal function is expected to begin in the third quarter of 2021.
- PHYOX-OBX: Enrollment in this observational study began in the third quarter of 2021 in participants with PH3 to evaluate the association between Uox excretion and the rate of kidney stone formation.

Other Key Nedosiran Activities

We expect the results from the PHYOX2 trial to support marketing authorization applications for the treatment of PH1 in the U.S. and other major markets and intend to submit a New Drug Application ("NDA") to the FDA in the fourth quarter of 2021.

The inconsistent data seen specifically in participants with PH2 have led us to make the strategic decision not to move forward with our plan to build Dicerna into a fully integrated commercial enterprise to support nedosiran. Instead, we intend to pursue commercial out-licensing opportunities to help ensure global access to nedosiran, subject to necessary approvals.

RG6346 for Chronic Hepatitis B Virus Infection

RG6346 is our GalXC RNAi product candidate for the treatment of chronic HBV infection. HBV is the world's most common serious liver infection and affects an estimated 300 million people worldwide. Chronic HBV infection is characterized by the presence of the HBV surface antigen ("HBsAg") for six months or more.

We are conducting a Phase 1 randomized, placebo-controlled, double-blind study to evaluate the safety and tolerability of RG6346 in healthy volunteers and in patients with non-cirrhotic chronic HBV. Secondary objectives of the study include characterization of the pharmacokinetic profile of RG6346 and evaluation of preliminary pharmacodynamic effects on markers of HBV antiviral efficacy, including reductions of HBsAg and HBV DNA levels in blood. The Phase 1 clinical trial is divided into three phases or groups:

- Group A is a single-ascending-dose arm in which 30 healthy volunteers received a dose of RG6346.
- Group B is a single-dose arm in which eight participants with chronic HBV who are naïve to nucleoside analog ("NUC") therapy received a 3.0 mg/kg dose of RG6346 or placebo.
- Group C is a multiple-ascending-dose arm in which RG6346 (1.5, 3.0, or 6.0 mg/kg) or placebo was administered to 18 participants with chronic HBV who are already being treated with NUCs.

In an effort to be optimally positioned to develop and commercialize RG6346 in combination with other novel drugs, we entered into the Roche Collaboration Agreement in October 2019. Under the terms of the agreement, we are leading the development of RG6346 through the current Phase 1 trial. Roche intends to further develop RG6346 and initiated RG6346 in a Roche-sponsored Phase 2 combination trial for the treatment of chronic HBV infection in March 2021. The Phase 2 platform trial will evaluate the efficacy and safety of RG6346 in combination with multiple additional agents with novel mechanisms of action, including standard of care nucleos(t)ide therapy and in triple combinations with pegylated interferon alfa-2a, Roche's novel investigational agents, core protein allosteric modulator ("CpAM") or TLR7 agonist.

Belcesiran (DCR-A1AT) for Alpha-1 Antitrypsin Deficiency-Associated Liver Disease

Our GalXC RNAi product candidate for the treatment of AATLD, belcesiran, is currently being tested in Phase 1 and Phase 2 clinical studies. AAT deficiency is a rare genetic condition caused by mutations in the *SERPINA1* gene that results in disease of the liver and lungs. AAT protein is produced in hepatocytes and circulates in the bloodstream; AAT protects the lungs and other parts of the body by neutralizing neutrophil elastase, an enzyme that fights infection but can also damage healthy tissues if not adequately regulated by AAT.

The majority of people with severe AAT deficiency are homozygous for the Z allele (PiZZ genotype). In the liver, misfolding of the mutant Z-AAT protein causes the protein to aggregate in liver cells, leading to liver injury, including fibrosis, cirrhosis, and hepatocellular carcinoma. Recent epidemiology research indicates that approximately 120,000 individuals in Europe and 63,000 individuals in the U.S. carry this ZZ genotype; the genotype occurs most frequently in individuals of Northern European descent. An estimated 10% or more of adults with AAT deficiency develop clinically meaningful liver disease, and recent research suggests that AATLD is both underrecognized and underdiagnosed. People with AAT deficiency may also develop lung disease, including

emphysema. AATLD can affect infants, children, and adults. Liver transplantation is currently the only effective treatment for AATLD.

Our Phase 1 trial of belcesiran is an ongoing placebo-controlled study designed to evaluate the safety and tolerability of single doses of belcesiran when administered to healthy adult participants. Secondary objectives are to characterize the pharmacokinetic profile of belcesiran and to evaluate the preliminary pharmacodynamic effects on serum AAT protein concentrations.

Data from an interim analysis announced in July 2021 of the four completed active-treatment dose cohorts (0.1, 1.0, 3.0, and 6.0 mg/kg) showed dose-dependent reductions in serum AAT with administration of a single dose of belcesiran. In this analysis, belcesiran was found to have an acceptable safety profile and was generally well tolerated. The final 12.0 mg/kg dose cohort in this trial is ongoing, and we plan to present additional data from this study at a medical congress in 2021, subject to abstract acceptance.

We initiated dosing in the Phase 2 trial of belcesiran in June 2021. The ESTRELLA Phase 2 trial is a randomized, multidose, double-blind, placebo-controlled trial evaluating the safety, tolerability, pharmacokinetics, and pharmacodynamics of belcesiran in adult participants with AATLD. The study includes a 24-week cohort and a 48-week cohort to be conducted in parallel, each with up to 27 participants who have a diagnosis of PiZZ-type AAT deficiency and AATLD.

DCR-AUD for Alcohol Use Disorder

We are currently pursuing development of DCR-AUD, an investigational therapy based on Dicerna's GalXC technology, for the treatment of alcohol use disorder ("AUD"). DCR-AUD is designed to specifically knock down *ALDH2* gene expression in the liver, which plays a key role in alcohol metabolism. ALDH2 mRNA knockdown may help individuals with AUD avoid harmful levels of alcohol use.

AUD is a chronic condition characterized by compulsive alcohol use, loss of control over alcohol use, and a negative emotional state when not using alcohol. A range of medical, psychological, social, economic, and personal problems are associated with AUD. It is estimated that more than 14 million adults in the U.S. are living with AUD. With nearly 100,000 deaths annually, it is one of the leading preventable causes of death in the U.S. Globally, AUD affects approximately 283 million people, according to the World Health Organization.

AUD is often undiagnosed and untreated. Of the more than 14 million individuals in the U.S. with AUD, fewer than 1.4 million received AUD treatment of any kind, including psychosocial support, while only 10% of these – or roughly 140,000 people – received medication to treat their disorder, presenting a significant opportunity for a therapeutic option that can help those with AUD achieve their individual treatment goals.

We received IND clearance from the FDA for DCR-AUD in July 2021 and plan to initiate a Phase 1 trial to evaluate the safety and tolerability of single ascending fixed doses of DCR-AUD in healthy volunteers in the third quarter of 2021.

Collaborative Program Updates

Eli Lilly and Company

During the second quarter of 2020, Lilly selected LY3819469, a GalXC molecule for the second collaboration target in cardiometabolic diseases, for advancement into preclinical development. In May 2021, the FDA accepted the IND application filed by Lilly for LY3819469, targeting the *LPA* gene as a potential treatment for cardiometabolic diseases, triggering a $10.0 million payment to Dicerna. We received this payment in the second quarter of 2021, and dosing in this Phase 1 clinical trial of LY3819469 began in June 2021. Two additional GalXC molecules, DCR-CM3 and DCR-CM4, are currently in preclinical development. Dicerna estimates that Lilly will file an IND for DCR-CM4 in the first quarter of 2022. IND/CTA filings under the Lilly Collaboration Agreement are the responsibility of Lilly and are at their discretion.

Lilly filed an IND and initiated a Phase 1 study of LY3561774, a GalXC molecule for the first collaboration target in cardiometabolic diseases that targets the *ANGPTL3* gene for the treatment of dyslipidemia, in the fourth quarter of 2020. As a result of this filing, we achieved a milestone associated with the first filing of an IND with the FDA, triggering a $10.0 million payment to us.

In February 2021, Lilly notified us of their decision to extend for an additional year the initial research collaboration term for the extrahepatic targets subject to the Lilly Collaboration Agreement. Under the agreement between the companies, Lilly has the option to extend the three-year initial research collaboration term for these extrahepatic targets for up to three consecutive one-year periods. This first extension allows the research program for these extrahepatic targets under the collaboration between the two companies to continue through October 2022.

Novo Nordisk

During the fourth quarter of 2020, Novo nominated its first candidate under the Novo Collaboration Agreement. Pursuant to the agreement, upon achievement of proof of principle of the first nominated candidate, Dicerna earned a $2.5 million milestone, which we received in February 2021. Also during the fourth quarter of 2020, Dicerna met its obligation to deliver GalXC molecules for a defined number of targets for the first year of the Novo Collaboration Agreement, entitling us to a $25.0 million payment. This payment was received in February 2021.

Roche

In March 2021, Roche initiated RG6346 in a Roche-sponsored Phase 2 combination trial for the treatment of chronic HBV infection, which entitled us to a $25.0 million milestone payment under the Roche Collaboration Agreement, which we received in the second quarter of 2021.

Boehringer Ingelheim

In May 2021, we announced that BI accepted a GalXC RNAi candidate for advancement under the BI Agreement, as amended and supplemented by the ATA, for the discovery and development of novel therapies for the treatment of chronic liver diseases. Acceptance of the DCR-LIV2 compound as a development candidate triggered a single-digit multimillion-dollar milestone payment to Dicerna, which we received and recognized in full in the second quarter of 2021. DCR-LIV2 will be evaluated for the treatment of nonalcoholic steatohepatitis (“NASH”), a chronic liver disease for which there are no approved therapeutic interventions.

Critical Accounting Policies and Significant Judgments and Estimates

Our discussion and analysis of our financial condition and results of operations is based on our condensed consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the U.S. The preparation of our condensed consolidated financial statements requires us to make estimates and apply judgments that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities as of the date of the condensed consolidated financial statements, as well as the revenue and expenses incurred during the reported periods. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances. Actual results may differ from these estimates and could have a material impact on our condensed consolidated financial statements.

The critical accounting policies that we believe impact significant judgments and estimates used in the preparation of our financial statements presented in this report are described in “Management’s Discussion and Analysis of Financial Condition and Results of Operations – Critical Accounting Policies and Significant Judgments and Estimates” in our Annual Report on Form 10-K filed with the SEC on February 26, 2021. There have been no significant changes to our critical accounting policies as disclosed in our most recently filed Annual Report on Form 10-K during the six months ended June 30, 2021.

Recent Accounting Pronouncements

A summary of significant recent accounting pronouncements that we have adopted or expect to adopt is included in Note 1 – Description of Business and Basis of Presentation to our condensed consolidated financial statements (see Part I, Item 1 – “Financial Statements” of this Quarterly Report on Form 10-Q).

Financial Operations Overview

Revenue

Our revenue to date has been generated primarily through research funding, license fees and other upfront payments, option exercise fees, milestone payments, and preclinical development activities, along with research activities under our research collaboration and license arrangements with Novo, Roche, Lilly, Alexion, and BI. We have not generated any commercial product revenue, nor do we expect to generate any material product revenue in the near-term.

In April 2021, we announced that Royalty Pharma had acquired our royalty interest in Alnylam’s OXLUMO (lumasiran) for an upfront cash payment of $180.0 million, which was received in April 2021, and up to $60.0 million in contingent sales-based milestone payments.

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 current or future collaborations with partners, and product sales from our internally developed products. We expect that any revenue we generate will fluctuate in future periods as a result of the timing of our or our collaborators’ achievement of preclinical, clinical, regulatory, and commercialization milestones, to the extent achieved, the timing and amount of any payments to us relating to such milestones, and the extent to which any of our product candidates are approved and successfully commercialized by us or a collaborator. Delays in or changes to the research and development plans and timelines related to our collaboration agreements are likely due to the COVID-19 pandemic.

Because we recognize the majority of our collaboration revenue on a cost-to-cost measure of progress, revenues recognized in the near-term may be lower than originally anticipated and could be recognized over an extended period of time as a result.

Research and development expenses

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

- direct research and development expenses incurred under arrangements with third parties, such as contract research organizations, contract manufacturing organizations, and consultants;
- platform-related expenses, including discovery research, lab supplies, license fees, and consultants;
- employee-related expenses, including salaries, benefits, and stock-based compensation expense; and
- facilities, depreciation, and other allocated expenses, which include direct and allocated expenses for rent, maintenance of facilities, and information technology; depreciation of leasehold improvements and equipment; and laboratory and other supplies.

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

Delays in or changes to our research and development plans and timelines, which impact both our internal and external resources, have occurred and may continue to occur due to the COVID-19 pandemic. Internally, throughout 2020 and into 2021, we were impacted by mandatory work from home edicts directed by the local governments in the jurisdictions in which we operate. However, essential work exemptions continued to permit critical research and development and laboratory activities for limited personnel. Those exemptions enabled some continued discovery research and activities supporting our collaborative agreements and our own programs. Externally, a number of our clinical trial sites have delayed and may continue to delay trial-related activities as a result of COVID-19 or its variants. Any of these factors could cause the timing of the research and development expenses we expect to incur to shift into later periods and have the potential to cause us to expend more funds than originally contemplated as a result of needing to extend clinical development activities.

General and administrative expenses

General and administrative expenses primarily consist of salaries and related benefits, including stock-based compensation, related to our executive, finance, legal, business development, commercial, and support functions. Other general and administrative expenses include travel expenses, professional legal fees, audit, tax, and other professional services, and allocated information technology and facility-related costs not otherwise included in research and development expenses. General and administrative expenses also included costs associated with Dicerna's previously planned strategy to commercialize nedosiran in the U.S. ourselves, if approved, and partner with a third party for other major markets outside of the U.S. However, based on inconsistent results observed in the PH2 subtype of patients included in our PHYOX2 pivotal study, we now plan to pursue commercial out-licensing opportunities to commercialize nedosiran in major markets including the U.S., subject to approvals. We expect general and administrative expenses to remain comparable with the three months ended June 30, 2021 as we cease our plans to build commercial operations in-house for nedosiran.

Delays in or changes to our research and development plans and timelines due to the COVID-19 pandemic may also impact our support functions, which could cause the timing of certain general and administrative expenses we expect to incur to shift into later periods.

Other income (expense)

Other income (expense) primarily consists of expense recorded for the derivative liability established for contingent royalty and milestone payments that may be owed to Alnylam in the future under the terms of the collaboration agreement between the parties. Other income (expense) also includes income recognized from the upfront payment from Royalty Pharma plc, interest income, and interest expense. Interest income consists of income earned on our cash and cash equivalents, held-to-maturity investments, and restricted cash equivalents. We expect that interest income will continue to decrease due to recent decreases in interest rates.

Provision for income taxes

Provision for income taxes primarily represents the estimated amount of U.S. federal tax payable not expected to be fully offset by any tax attributes.

Results of Operations

Comparison of the Three and Six Months Ended June 30, 2021 and 2020

The following table summarizes the results of our operations for the periods indicated (amounts in thousands, except percentages):

	THREE MONTHS ENDED JUNE 30,			
	2021	2020	$ CHANGE	% CHANGE
Revenue	$ 41,337	$ 40,448	$ 889	2.2 %
Operating expenses:				
Research and development	56,119	53,376	2,743	5.1 %
General and administrative	25,462	20,565	4,897	23.8 %
Total operating expenses	81,581	73,941	7,640	10.3 %
Loss from operations	(40,244)	(33,493)	(6,751)	20.2 %
Other income (expense):				
Interest income	111	1,729	(1,618)	(93.6)%
Interest expense	(4)	(6)	2	(33.3)%
Other expense, net	(132)	(50)	(82)	164.0 %
Total other (expense) income	(25)	1,673	(1,698)	(101.5)%
Loss before income taxes	(40,269)	(31,820)	(8,449)	26.6 %
Provision for income taxes	(546)	—	(546)	(100.0)%
Net loss	$ (40,815)	$ (31,820)	$ (8,995)	28.3 %

	SIX MONTHS ENDED JUNE 30,			
	2021	2020	$ CHANGE	% CHANGE
Revenue	$ 88,940	$ 74,476	$ 14,464	19.4 %
Operating expenses:				
Research and development	112,157	96,547	15,610	16.2 %
General and administrative	46,134	36,588	9,546	26.1 %
Total operating expenses	158,291	133,135	25,156	18.9 %
Loss from operations	(69,351)	(58,659)	(10,692)	18.2 %
Other income (expense):				
Interest income	391	4,342	(3,951)	(91.0)%
Interest expense	(8)	(10)	2	(20.0)%
Other (expense) income	(1,266)	15	(1,281)	*
Total other (expense) income	(883)	4,347	(5,230)	(120.3)%
Loss before income taxes	(70,234)	(54,312)	(15,922)	29.3 %
Provision for income taxes	(546)	—	(546)	(100)%
Net loss	$ (70,780)	$ (54,312)	$ (16,468)	30.3 %

* Percentage change not meaningful

Revenue

The following table provides a summary of revenue recognized (amounts in thousands):

	THREE MONTHS ENDED JUNE 30,			
	2021	2020	$ CHANGE	% CHANGE
Novo	$ 6,700	$ 2,447	$ 4,253	173.8 %
Roche	14,234	20,677	(6,443)	(31.2)%
Lilly	14,735	9,487	5,248	55.3 %
Alexion	2,487	7,063	(4,576)	(64.8)%
BI	3,181	774	2,407	311.0 %
Total	$ 41,337	$ 40,448	$ 889	2.2 %

	SIX MONTHS ENDED JUNE 30,			
	2021	2020	$ CHANGE	% CHANGE
Novo	$ 13,312	$ 4,052	$ 9,260	228.5 %
Roche	39,845	39,984	(139)	(0.3)%
Lilly	22,298	19,069	3,229	16.9 %
Alexion	10,304	9,825	479	4.9 %
BI	3,181	1,546	1,635	105.8 %
Total	$ 88,940	$ 74,476	$ 14,464	19.4 %

Dicerna receives cash in the form of upfront, milestone, and reimbursement payments from its collaboration partners. However, except for BI, upfront payments received are typically recognized as revenue over time, as revenue from Dicerna's collaboration partners is recognized on a cost-to-cost measure of progress. As a result, the amount of revenue Dicerna recognizes each period is directly correlated with the amount of services performed during the period.

Revenue was relatively flat for the three months ended June 30, 2021 compared to the same period in 2020, as increases in Lilly, Novo, and BI revenues were largely offset by decreases in Roche and Alexion revenues. The increases in Lilly, Novo, and BI revenues during the three months ended June 30, 2021 reflect a cumulative catch-up in Lilly revenue due to the $10.0 million milestone achieved in the second quarter of 2021, increased services performed under the collaboration agreement with Novo, and achievement of the milestone associated with BI's acceptance of the DCR-LIV2 compound as a development candidate, respectively. The decrease in Roche revenue in the three months ended June 30, 2021 is due to changes in total estimated costs, as well as fewer services performed compared to the same period in the prior year. In addition, revenue for the three months ended June 30, 2021 was impacted by a decrease in services provided to Alexion due to the uncertainty regarding this research program as a result of AstraZeneca plc's acquisition of Alexion.

The increase in revenue for the six months ended June 30, 2021 is primarily attributable to increases in services performed under the collaboration agreement with Novo, as well as under the Lilly collaboration agreement.

Research and development expenses

The following table summarizes our research and development expenses incurred during the periods indicated (amounts in thousands, except percentages):

	THREE MONTHS ENDED JUNE 30,			
	2021	2020	$ CHANGE	% CHANGE
Belcesiran direct research and development expenses	$ 3,842	$ 4,070	$ (228)	(5.6)%
Nedosiran direct research and development expenses	10,382	9,220	1,162	12.6 %
Partner and remaining core programs direct research and development expenses	10,753	18,515	(7,762)	(41.9)%
Total direct research and development expenses	$ 24,977	$ 31,805	$ (6,828)	(21.5)%
Platform-related and discovery research expenses	4,698	3,146	1,552	49.3 %
Employee-related expenses	19,182	15,386	3,796	24.7 %
Facilities, depreciation, and other expenses	7,262	3,039	4,223	139.0 %
Total	$ 56,119	$ 53,376	$ 2,743	5.1 %

	SIX MONTHS ENDED JUNE 30,			
	2021	2020	$ CHANGE	% CHANGE
Belcesiran direct research and development expenses	$ 7,072	$ 9,028	$ (1,956)	(21.7)%
Nedosiran direct research and development expenses	20,352	16,758	3,594	21.4 %
Partner and remaining core programs direct research and development expenses	22,980	29,404	(6,424)	(21.8)%
Total direct research and development expenses	$ 50,404	$ 55,190	$ (4,786)	(8.7)%
Platform-related and discovery research expenses	9,432	6,645	2,787	41.9 %
Employee-related expenses	39,386	28,876	10,510	36.4 %
Facilities, depreciation, and other expenses	12,935	5,836	7,099	121.6 %
Total	$ 112,157	$ 96,547	$ 15,610	16.2 %

Research and development expenses increased $2.7 million for the three months ended June 30, 2021 compared to the three months ended June 30, 2020 primarily due to a $4.2 million increase in facilities, depreciation, and other expenses and a $3.8 million increase in employee-related expenses, which includes salaries, benefits, and stock-based compensation. The increases in facilities-related expenses, which include information technology expenses, and employee-related expenses are the result of an increase in research and development headcount necessary to support our expanding pipeline and collaboration agreements. These increases were offset by a $6.8 million decrease in direct research and development expenses. Direct research and development expenses include expenses incurred under arrangements with third parties, such as contract research organizations, contract manufacturing organizations, and consultants. The decrease in direct research and development expenses was primarily driven by $2.6 million decreases in both Alexion and internal direct research and development expenses, both of which were primarily the result of decreases in drug substance expense.

Research and development expenses increased $15.6 million for the six months ended June 30, 2021 compared to the six months ended June 30, 2020 primarily due to $10.5 million increase in employee-related expenses. Research and development expenses were also impacted by a $7.1 million increase in facilities, depreciation, and other expenses, which includes information technology expenses, in the six months ended June 30, 2021. Both increases in employee-related expenses and facilities-related expenses are the result of an increase in research and development headcount necessary to support our expanding pipeline and collaboration agreements.

We expect our overall research and development expenses to continue to increase for the foreseeable future as we ramp our clinical manufacturing activities, continue clinical activities associated with our core product candidates, and continue activities under our existing collaboration agreements.

General and administrative expenses

General and administrative expenses were $25.5 million and $20.6 million for the three months ended June 30, 2021 and 2020, respectively. The $4.9 million increase for the three months ended June 30, 2021 is primarily due to a $3.5 million increase in professional consulting services in the three months ended June 30, 2021.

General and administrative expenses were $46.1 million and $36.6 million for the six months ended June 30, 2021 and 2020, respectively. The $9.5 million increase for the six months ended June 30, 2021 is primarily due to a $5.0 million increase in professional consulting services. In addition, general and administrative expenses increased $2.2 million due to employee-related expenses as a result of an increase in general and administrative headcount necessary to support our expanding pipeline and collaboration agreements.

We expect general and administrative expenses to remain comparable with the three months ended June 30, 2021 as we cease our plans to build commercial operations in-house for nedosiran.

Liquidity and Capital Resources

Overview

We have historically funded our operations primarily through the public offering and private placement of our securities and consideration received from our collaborative arrangements with Novo, Roche, Lilly, Alexion, and BI. As of June 30, 2021, we had cash and cash equivalents and held-to-maturity investments of $709.6 million compared to $568.8 million as of December 31, 2020.

In February 2020, we issued and sold an aggregate of approximately $40.0 million of shares of our common stock to a single institutional investor pursuant to our common stock Sales Agreement with Cowen and Company, LLC as the sales agent. In this transaction, we sold an aggregate of 2,077,500 shares of common stock at a price of $19.25 per share, resulting in net proceeds of approximately $39.2 million after a deduction of approximately $0.8 million in sales commissions. The shares in the offering were sold pursuant to a shelf registration statement declared effective by the SEC on May 31, 2018 and a prospectus supplement filed with the SEC on June 1, 2018.

In April 2021, we received an $180.0 million upfront payment from the sale of our royalty interest in Alnylam's OXLUMO (lumasiran) to Royalty Pharma.

Payments received from our collaboration partners during the three and six months ended June 30, 2021 were as follows (amounts in thousands):

	THREE MONTHS ENDED JUNE 30, 2021	SIX MONTHS ENDED JUNE 30, 2021
Novo	107	$ 27,607
Roche	26,102	27,852
Lilly	10,094	10,779
Alexion	2,798	5,209
BI	2,525	3,092
Total	$ 41,626	$ 74,539

Payments received from our collaboration partners during the three and six months ended June 30, 2020 were as follows (amounts in thousands):

	THREE MONTHS ENDED JUNE 30, 2020	SIX MONTHS ENDED JUNE 30, 2020
Novo	$ —	$ 175,000
Roche	—	200,000
Alexion	15,000	15,094
BI	—	260
Total	$ 15,000	$ 390,354

We believe that our cash, cash equivalents, held-to-maturity investments, and anticipated milestones and other payments from existing collaborators provide us with sufficient resources to continue our planned operations and clinical activities into 2025.

On May 6, 2021, we entered into a Sales Agreement with Cowen and Company, LLC, as sales agent, to provide for the offering, issuance, and sale by us of up to $200.0 million of our common stock from time to time, including in "at-the-market" offerings under our universal shelf registration statement on Form S-3 that we filed on November 7, 2019. Under the at-the-market facility, the sales agent is entitled to be compensated in an amount of up to 3.0% of the gross proceeds from sales of our common stock.

Cash flows

The following table shows a summary of our condensed consolidated cash flows for the periods indicated (amounts in thousands):

	SIX MONTHS ENDED JUNE 30,	
	2021	2020
Net cash provided by operating activities	$ 132,137	$ 279,424
Net cash used in investing activities	$ (55,721)	$ (278,384)
Net cash provided by financing activities	$ 18,027	$ 45,614

Operating activities

Net cash provided by operating activities decreased $147.3 million in the six months ended June 30, 2021 compared to the six months ended June 30, 2020, primarily due to a $168.8 million decrease in contract receivables, largely due to the upfront cash payment received from Roche in January 2020 in connection with our collaboration agreement, and a $163.2 million decrease in deferred revenue. These decreases were partially offset by a $179.8 million increase in deferred income associated with the upfront payment received from Royalty Pharma in April 2021.

Investing activities

Net cash used in investing activities decreased $222.7 million in the six months ended June 30, 2021 compared to the six months ended June 30, 2020, primarily due to a $137.5 million decrease in purchases of held-to-maturity investments for the six months ended June 30, 2021, as the comparable period in the prior year reflected an increased cash balance from the Novo and Roche upfront payments available for purchases. In addition, there was a $90.0 million increase in maturities of investments.

Financing activities

Net cash provided by financing activities for the six months ended June 30, 2021 decreased $27.6 million compared to the six months ended June 30, 2020. The decrease was primarily due to the receipt of $39.2 million in net proceeds in February 2020 from the private placement of our common stock, which was partially offset by a $13.4 million increase in proceeds received from the exercise of stock options.

Funding requirements

We expect that our primary uses of capital will be for third-party clinical research and development services and manufacturing costs; compensation and related expenses; laboratory and related supplies; legal and other regulatory expenses; and general overhead costs. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates and the extent to which we may enter into additional collaborations with third parties to participate in their development and commercialization, we are unable to estimate the amounts of capital outlays and operating expenditures associated with our anticipated development activities. However, based on our current operating plan, we believe that our available cash, cash equivalents, held-to-maturity investments, and anticipated milestone and other payments from existing collaborations will be sufficient to fund the execution of our current clinical and operating plans into 2025. We based this estimate on assumptions that may prove to be incorrect, and we could utilize our available capital resources sooner than we currently expect. In addition, for the year ending December 31, 2021, we forecast receiving $83.0 million in cash from our collaborations, including anticipated milestone achievement, based on the current terms in our collaboration agreements and anticipated timing of development in our programs covered by such collaborations. $74.5 million of this amount was received in the first six months of 2021. There can be no assurance that we will actually receive such payments under our collaboration agreements.

Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially as a result of a number of factors. Our future capital requirements are difficult to forecast and will depend on many factors, including:

- the potential receipt of any milestone payments under the Novo Collaboration Agreement, Roche Collaboration Agreement, Lilly Collaboration Agreement, Alexion Collaboration Agreement, BI Agreements, Alnylam Collaboration Agreement, and the Royalty Pharma plc agreement;
- the terms and timing of any other collaboration, licensing, and other arrangements that we may establish;
- the initiation, progress, timing, and completion of preclinical studies and clinical trials for our current and future potential product candidates, including the impact of COVID-19 or its variants on our ongoing and planned research and development efforts;
- our alignment with the FDA on regulatory approval requirements;
- the impact of COVID-19 or its variants on the operations of key governmental agencies, such as the FDA, which may delay the development of our current product candidates or any future product candidates;
- the number and characteristics of product candidates that we pursue;
- the outcome, timing, and cost of regulatory approvals;
- delays that may be caused by changing regulatory requirements;
- the cost and timing of hiring new employees to support our continued growth;
- the costs involved in filing and prosecuting patent applications and enforcing and defending patent claims;
- the costs of filing and prosecuting intellectual property rights and enforcing and defending any intellectual property-related claims;
- the costs of responding to and defending ourselves against complaints and potential litigation;
- the costs and timing of procuring clinical and commercial supplies for our product candidates;
- the extent to which we acquire or in-license other product candidates and technologies; and
- the extent to which we acquire or invest in other businesses, product candidates, or technologies.

Until such time, if ever, that we generate significant product revenue, we expect to finance our future cash needs through a combination of public or private equity offerings, debt financings, royalty stream monetization, and research collaboration and license agreements.

Please see the risk factors set forth in Part II, Item 1A – “Risk Factors” in this Quarterly Report on Form 10-Q for additional risks associated with our substantial capital requirements.

Contractual Obligations and Commitments

The following is a summary of our contractual obligations as of June 30, 2021 (amounts in thousands):

	Payments Due By Period*				
	Total	Less Than 1 Year	More Than 1 Year and Less Than 3 Years	More Than 3 Years and Less Than 5 Years	More Than 5 Years
Operating lease obligations	$ 67,846	$ 7,668	$ 17,472	$ 18,536	$ 24,170
Finance lease obligations	$ 212	$ 64	$ 120	$ 28	$ —

* Represents future minimum lease payments under our existing non-cancelable operating leases for our offices and laboratory space and our finance lease for equipment.

We have obligations to make future payments to licensors that become due and payable on the achievement of certain development, regulatory, and commercial milestones. We have not included any such potential obligations on our condensed consolidated balance sheets since the achievement and timing of these milestones were not probable or estimable as of June 30, 2021.

Off-Balance Sheet Arrangements

As of June 30, 2021, we did not have any relationships with unconsolidated entities or financial partnerships, such as entities often referred to as "special purpose" entities, which would have been established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purposes.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

The primary objectives of our investment activities are to ensure liquidity and to preserve principal, while at the same time maximize 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 June 30, 2021, we had cash, cash equivalents, and held-to-maturity investments of $709.6 million. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the low risk profile of our investments, an immediate 100 basis point change in interest rates by the U.S. federal reserve would not have a material effect on the fair market value of our cash and cash equivalents or held-to-maturity investments. To minimize the risk in the future, we intend to maintain our portfolio of cash, cash equivalents, and held-to-maturity investments in a variety of securities, including commercial paper, money market funds, and government securities.

ITEM 4. CONTROLS AND PROCEDURES

Disclosure Controls and Procedures

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

As of the end of the period covered by this Quarterly Report on Form 10-Q, we carried out an evaluation, under the supervision and with the participation of our management, including the chief executive officer and the chief financial officer, who serve as our principal executive officer and principal financial officer, respectively, of the effectiveness of the design and operation of our disclosure controls and procedures pursuant to Exchange Act Rule 13a-15. Based upon, and as of the date of, this evaluation, our chief executive officer and our chief financial officer concluded that our disclosure controls and procedures were effective. Accordingly, management believes that the financial statements included in this report fairly present in all material respects our financial condition, results of operations, and cash flows for the periods presented.

Changes in Internal Control Over Financial Reporting

We continuously seek to improve the efficiency and effectiveness of our internal controls. This results in refinements to processes throughout the Company. There were no changes in the Company's internal control over financial reporting that occurred during the quarter ended June 30, 2021 in connection with management's evaluation required by Exchange Act Rules 13a-15(f) and 15d-15(f), that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Due to the COVID-19 pandemic, in March 2020, certain employees of the Company began working (and continue to work) remotely. The Company has not identified any material changes in the Company's internal control over financial reporting as a result of these changes to the working environment. The Company is continually monitoring and assessing the COVID-19 situation to determine any potential impacts on the design and operating effectiveness of our internal controls over financial reporting.

Inherent Limitations on the Effectiveness of Controls

Our management, including the chief executive officer and chief financial officer, does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent all error and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within a company have been detected. These inherent limitations include the realities that judgments in decision-making can be faulty and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people, or by management override of the controls. The design of any system of controls also is based, in part, upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions. Over time, controls may become inadequate because of changes in conditions, or the degree of compliance with the policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

PART II: OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

From time to time, we may be subject to legal proceedings, claims, and litigation arising in the ordinary course of business. We are not currently a party to or aware of any proceedings that we believe will have, individually or in the aggregate, a material adverse effect on our business, financial condition, or results of operations. Any future litigation could result in substantial costs and divert our management's attention and resources, which could cause serious harm to our business, operating results, and financial condition. We maintain liability insurance; however, if any costs or expenses associated with litigation exceed our insurance coverage, we may be forced to bear some or all of these costs or expenses directly, which could be substantial.

ITEM 1A. RISK FACTORS

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

Risks Related to Our Business and Strategy

Business interruptions resulting from the coronavirus disease (COVID-19) outbreak or similar public health crises could cause a disruption of the development of our product candidates and adversely impact our business.

Public health crises such as pandemics or similar outbreaks could adversely impact our business. In December 2019, a novel strain of a virus named SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), or coronavirus, which causes coronavirus disease "COVID-19" was reported to have surfaced in Wuhan, China and has reached multiple other regions and countries, including Lexington, Massachusetts, where our primary offices and laboratory space are located, and in Boulder, Colorado, where we also have office and laboratory space. The coronavirus pandemic is evolving, and to date has led to the implementation of various responses, including government-imposed quarantines, travel restrictions, and other public health safety measures. It is difficult to predict what the lasting impact of the pandemic will be, and what the impact might be if the Company or any of the third parties with whom it engages were to experience additional shutdowns or other prolonged business disruptions. New strains of COVID-19 and its variants were reported in different parts of the world and have since reached the U.S. Depending on the duration and impact of the resurgence and new strains of COVID-19 or its variants and depending on where the infections rates are highest, the Company's business, results of operations, and financial condition may be negatively impacted, including on the ability of regulators to continue ensuring the timely review and approval of applications. For example, as of June 23, 2020, the U.S. Food and Drug Administration ("FDA") noted it is continuing to ensure timely reviews of applications for medical products during the COVID-19 pandemic in line with its user fee performance goals; however, the FDA may not be able to continue its current pace and approval timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and, due to the COVID-19 pandemic and travel restrictions, the FDA is unable to complete such required inspections during the review period. In 2020, several companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. The Company's ability to conduct its business in the manner and on the timelines presently planned could have a material adverse impact on the Company's business, results of operations, and financial condition. In addition, the recurrence or resurgence of COVID-19 cases, including new strains of COVID-19 or its variants, could cause other widespread or more severe impacts depending on where infection rates are highest. While certain vaccines and treatments for COVID-19 have been authorized for use, some in emergency cases, there can be no assurance that such measures will help or slow the progression of the COVID-19 virus or its variants in all territories in a significant manner or at all.

In many of the territories in which we operate our clinical trials, the COVID-19 pandemic has impacted and, with new strains of COVID-19 and its variants, may continue to impact enrollment and dosing in certain of the clinical trials of our product candidates, as well as changes in our business generally, including:

- diversion of healthcare resources away from the conduct of clinical trials to focus on pandemic concerns, including the attention of physicians serving as our clinical trial investigators, hospitals serving as our clinical trial sites, and hospital staff supporting the conduct of our clinical trials, including, for example, the interruption of enrollment of participants in clinical studies where enrollment involves interactions with participants at hospitals or medical facilities during the COVID-19 pandemic at some of our clinical trial sites;
- the potential for delay and disruption of the conduct of our clinical studies; for example, the potential for future delays or disruptions of our studies of belcesiran (formerly DCR-A1AT) and nedosiran;
- limitations on travel that have interrupted key trial activities, such as clinical trial site initiations and monitoring, domestic and international travel by employees, contractors, or patients to clinical trial sites, including any government-imposed travel restrictions or quarantines that may impact the ability or willingness of patients, employees, or contractors to travel to our clinical trial sites or secure visas or entry permissions, any of which could delay or adversely impact the conduct or progress and monitoring of our clinical trials;
- the interruption in global shipping affecting the transport of clinical trial materials, such as patient samples, investigational drug product, and other supplies used in our clinical trials;
- business disruptions caused by workplace, laboratory, and office closures, and an increased reliance on employees working from home, disruptions to or delays in ongoing laboratory experiments and operations, staffing shortages, travel

limitations or mass transit disruptions, any of which could adversely impact our business operations, impair the productivity of our personnel, subject us to additional cybersecurity risks, create data accessibility problems, cause us to become more susceptible to communication disruptions, or delay necessary interactions with local regulators, ethics committees, and other important agencies and contractors; and

- the demand of fill and finish capacity of final product by manufacturers producing COVID-19 vaccine products, and U.S. government exercise of its Defense Product Act authorities to mandate priority rated orders for production of vaccines or other supplies, could disrupt or delay the production of injectable medicines in the next 12-18 months, including our future scheduling of production runs for our and our collaborative partners' product candidates.

Three vaccines for COVID-19 were granted Emergency Use Authorization by the FDA in late 2020 and early 2021, and more are likely to be authorized in the coming months. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Protection Act, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials.

These and other factors arising from the coronavirus could worsen in countries that are already impacted by the coronavirus or could continue to spread to additional countries, each of which could further adversely impact our ability to conduct clinical trials and our business generally and could have a material adverse impact on our operations and financial condition and results.

We will need substantial funds to advance development of our product candidates and to commercialize any product candidates that receive marketing approval, and we cannot guarantee that we will have sufficient funds available in the future to develop and commercialize our current or future product candidates. Raising additional funds may cause dilution to our stockholders, restrict our operations, or require us to relinquish control over our technologies or product candidates.

We will need substantial funds to expand our development, regulatory, manufacturing, marketing, sales, and general and administrative operations 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, 2021, we had $709.6 million in cash, cash equivalents, and held-to-maturity investments. Based on our current operating plan and liquidity, we believe that our available cash, cash equivalents, held-to-maturity investments, and anticipated milestone and other payments from existing collaborations will be sufficient to fund the execution of our current clinical and operating plan into 2025. However, to the extent our clinical and operating plan changes, we will need to raise substantial additional funds. Further, our future capital requirements and the period for which our existing resources are able to support our operations may vary significantly from what we expect. Our 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, marketing approval, and commercialization of product candidates, if approved. 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 and manage the increased time to complete development of some programs due to the COVID-19 pandemic;
- 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 of our product candidates;
- to establish and maintain a commercialization infrastructure for any product candidates that receive marketing approval that we intend to commercialize independently;
- to obtain additional capital to support and expand our operations;
- to satisfy the requirements for quality and safety in developing and commercializing our products; 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 development or commercialization 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 or royalties in the near-term, if at all, and milestone payments, if any, are based on third-party determinations and/or events outside our control. Our revenue sources currently are, and will remain, 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, research collaborations and license agreements, 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, royalty stream monetization, 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, 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.

In April 2021, we entered into a royalty monetization arrangement with Royalty Pharma, pursuant to which, we sold our right to receive sales-based royalty payments on worldwide net sales of OXLUMO pursuant to the Patent Cross-License Agreement, dated as of April 3, 2020, by and between us and Alnylam Pharmaceuticals, Inc. (“Alnylam”). As consideration for the arrangement, we received $180.0 million upfront in cash and may receive up to $60.0 million in contingent sales-based milestone payments. As a result, we will no longer derive cash from royalty payments from sales of OXLUMO, other than in the form of contingent milestone payments under the royalty purchase agreement.

We have a history of operating losses; we 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 ribonucleic acid 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 RNAi molecules and delivery technologies. We have had significant operating losses since our inception related to expenses for our research and development and our ongoing operations and we expect to incur such losses for the foreseeable future. As of June 30, 2021, we had an accumulated deficit of $708.8 million. For the six months ended June 30, 2021 and for the years ended December 31, 2020, 2019, and 2018, our net losses were $70.8 million, $112.7 million, $120.5 million, and $88.9 million, respectively. Our technologies and product candidates are in varied 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 in the near-term, and we expect to continue to incur significant operating losses for the foreseeable future due to the cost of research and development, preclinical studies and clinical trials, and the regulatory approval process for product candidates. The amount of future losses is uncertain. Our ability to achieve profitability, if ever, will depend on, among other things, us or our existing collaborators, or any future collaborators, successfully developing product candidates, obtaining regulatory approvals to market and commercialize product candidates, manufacturing any approved products on commercially reasonable terms, establishing a sales and marketing organization or suitable third-party alternatives for any approved product, and raising sufficient funds to finance business activities. If we or our existing collaborators, or any future collaborators, are unable to develop and commercialize one or more of our product candidates or if sales revenue from any product candidate that receives approval is insufficient, we will not achieve profitability, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

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

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

- variations in the level of expense related to our product candidates or future development programs;
- additional unanticipated variations in the level of expenses due to the impact of the COVID-19 pandemic, including new strains of COVID-19 or its variants, on the timing of programs and the timing of availability of resources to deploy on such programs;

- delays in enrolling subjects in, initiating, conducting, or releasing 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 collaborators or licensors;
- 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;
- delays in engagement of our third-party manufacturers for our product candidates or their failure to execute on our manufacturing requirements or perform in accordance with current good manufacturing practices ("cGMP");
- timing of regulatory decisions and 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;
- delays or suspensions of clinical development or interruption of the supply chain associated with COVID-19, which have impacted and may continue to impact global healthcare systems and our trial sites' conduct of clinical trials, such as we have seen or may see in the nedosiran and belcesiran studies;
- 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 technology 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 cardiometabolic diseases and viral diseases. We are also exploring new applications of our RNAi technology with GalXC-Plus, which is designed to expand on the functionality and application of our flagship liver-based GalXC technology yet has the potential to treat diseases across multiple therapeutic areas. We believe that product candidates identified with our drug discovery and delivery platform may offer an improved therapeutic approach over 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 and GalXC-Plus is both preliminary and limited.

Relatively few product candidates based on RNAi have been tested in animals or humans, and a number of clinical trials conducted by other companies using RNAi technologies have not been successful. We may discover that GalXC and GalXC-Plus do 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 may spend substantial funds attempting to introduce these properties and may never succeed in doing so. In addition, product candidates based on GalXC and GalXC-Plus may demonstrate different chemical and pharmacological properties in patients than they do in laboratory studies. Even if product candidates, such as nedosiran, RG6346, belcesiran, and DCR-AUD have had successful results in animal studies and models, 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 and other regulatory authorities outside the U.S. have relatively limited experience with RNAi or GalXC-based therapeutics. 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 or GalXC-Plus prove to be ineffective, unsafe, or commercially unviable, our entire platform and pipeline would have little, if any, value, which would have a material adverse effect on our business, financial condition, results of operations, and prospects.

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

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

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

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

If a product candidate that has orphan drug designation subsequently receives the first FDA approval for the indication for that designation, the product candidate is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug 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 drug for the same indication as defined by the FDA.

Even if we, or any future collaborators, obtain orphan drug exclusivity for a product, such as we obtained in March 2020 for belcesiran for the treatment of alpha-1 antitrypsin (“AAT”) deficiency (“AATD”), that exclusivity may not effectively protect the

product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective, or makes a major contribution to patient care.

On August 3, 2017, the U.S. Congress passed the FDA Reauthorization Act of 2017 ("FDARA"). FDARA, among other things, codified the FDA's preexisting regulatory interpretation, to require that a drug Sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease to receive orphan drug exclusivity. The law reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. Moreover, in the Consolidated Appropriations Act of 2021, Congress did not further change this interpretation when it clarified that the interpretation codified in FDARA would apply in cases where the FDA issued an orphan designation before the enactment of FDARA but where product approval came after the enactment of FDARA. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

As in the U.S., we may apply for designation of a product candidate as an orphan drug for the treatment of a specific indication in the EU before the application for marketing authorization is made. For example, in August 2018, the European Medicines Agency ("EMA")'s Committee for Orphan Medicinal Products ("COMP") designated nedosiran as an orphan medicinal product for the treatment of primary hyperoxaluria ("PH") in the EU. In March 2020, the FDA granted orphan drug designation to belcesiran for the treatment of AATD. In December 2019, the European Commission granted orphan drug designation to belcesiran for the treatment of congenital AATD based on a positive opinion from the COMP of the EMA. Sponsors of orphan drugs in the EU can enjoy economic and marketing benefits, including up to 10 years of market exclusivity for the approved indication. During such period, marketing authorization applications for a "similar medicinal product" will not be accepted, unless another applicant can show that its product is safer, more effective, or otherwise clinically superior to the orphan-designated product. In the EU, a "similar medicinal product" is a medicinal product containing a similar active substance or substances as contained in a currently authorized orphan medicinal product, and which is intended for the same therapeutic indication. The respective orphan designation and exclusivity frameworks in the U.S. and in the EU are subject to change, and any such changes may affect our ability to obtain U.S. or EU orphan designations in the future.

Our product candidates are in varied stages of development and may fail or suffer delays that materially and adversely affect their commercial viability and/or our strategy with respect to seeking regulatory approval.

We currently have no products on the market and our product candidates are in varied stages of development. While our lead product candidate, nedosiran, is currently in registrational studies, there can be no assurance that data generated from such studies will support marketing approval for such product candidate in any indication for which we have evaluated nedosiran to date. For example, while we are evaluating nedosiran in the PH1, PH2, and PH3 subpopulations, we recently announced our plans to submit an NDA for nedosiran for the treatment of PH1 in the fourth quarter of 2021. In addition, there can be no assurance that the FDA will accept the NDA for review; nor is it certain that we will seek marketing approval for any additional indications for which we have evaluated nedosiran to date, nor can there be any assurance that the FDA will approve this product candidate for any indications for which we seek approval. Furthermore, seeking a more limited label reduces the potential market for a product candidate, even if it is approved. Our ability to achieve and sustain profitability depends on obtaining regulatory approvals, including Institutional Review Board ("IRB") or ethics committee approval, to conduct clinical trials at particular sites, successfully completing our clinical trials, and successfully commercializing our product candidates, either alone or with third parties, such as our collaborators. 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 of our product candidates in humans. Preclinical testing and clinical trials are expensive, difficult to design and implement, can take many years to complete, and are uncertain as to outcome. The start or end of a clinical study is often delayed or halted due to changing regulatory requirements, manufacturing challenges, required clinical trial administrative actions, slower than anticipated patient enrollment, changing standards of care, availability or prevalence of use of a comparative drug or required prior therapy, clinical outcomes, and financial constraints. For instance, delays or difficulties in patient enrollment or difficulties in retaining trial participants can result in increased costs, longer development times, or termination of a clinical trial. Clinical trials of a new product candidate require the enrollment of a sufficient number of patients, including patients who are suffering from the disease the product candidate is intended to treat and who meet other eligibility criteria. Rates of patient enrollment are affected by many factors, including the size of the patient population, the eligibility criteria for the clinical trial, the age and condition of the patients, the stage and severity of disease, the nature of the protocol, the proximity of patients to clinical sites, and the availability of effective treatments for the relevant disease. Thus, enrollment of sufficient patients can be challenging for rare disease drug development programs where patient populations are inherently small in size, particularly when there are competitive clinical trials. Due to the COVID-19 pandemic, we have experienced delays in enrollment and dosing in certain of our clinical trials for our product candidates and this risk of delays remains ongoing.

A product candidate can unexpectedly fail at any stage of preclinical and clinical development. The historical failure rate for product candidates is high due to many factors, including scientific feasibility, safety, efficacy, and changing standards of medical care. The results from preclinical testing or early clinical trials of a product candidate may not predict the results that will be obtained in later phase clinical trials of the product candidate. For example, results from our PHYOX2 pivotal trial of nedosiran for the PH2 subtype showed inconsistent reduction in urinary oxalate, despite prior nonclinical and clinical experience, suggesting more complexity in the PH2 disease biology than has been previously understood.

We, the FDA or other applicable regulatory authorities, an individual IRB with respect to its institution, or an independent ethics committee may suspend clinical trials of a product candidate at any time for various reasons, including a belief that individuals participating in such trials are being exposed to unacceptable health risks or adverse side effects. We may not have the financial resources to continue development of, or to enter into collaborations for, a product candidate if we experience any problems or other unforeseen events that delay or prevent regulatory approval of, or our ability to commercialize, product candidates, including:

- negative, inconclusive, or noncompetitive 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, revisit our strategy, or abandon a program;
- serious and unexpected drug-related side effects experienced by participants using our products in our clinical trials or by individuals using drugs similar to our product candidates;
- delays in submitting investigational new drug (“IND”) or comparable foreign applications or delays or failures in obtaining the necessary approvals from regulators or IRBs to commence a clinical trial, or a suspension or termination of a clinical trial once commenced;
- conditions imposed by the FDA or comparable foreign authorities, such as the EMA, regarding the scope or design of our clinical trials;
- competition for subjects in competitive clinical trials and delays in enrolling individuals in clinical trials;
- high drop-out rates of study participants;
- inadequate supply or quality of drug product or product candidate components or materials or other supplies necessary for the conduct of our clinical trials;
- greater than anticipated clinical trial costs;
- poor effectiveness of our product candidates during clinical trials;
- unfavorable FDA or other regulatory agency inspection of a manufacturing or clinical trial site or the inability to complete any required inspections during the review of any marketing application;
- failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;
- delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular, including, for example, compliance with FDA and other regulatory requirements associated with the COVID-19 pandemic; and
- varying interpretations of data by the FDA and foreign regulatory agencies.

Breakthrough Therapy Designation by the FDA may not actually lead to a faster development or regulatory review or approval process.

The FDA has granted Breakthrough Therapy Designation to nedosiran for the treatment of patients with PH type 1 (“PH1”). A breakthrough therapy is defined 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 currently approved therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA are also eligible for accelerated approval and priority review.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe a product candidate we develop meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of Breakthrough Therapy Designation may not result in a faster development process, review, or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate

approval by the FDA. In addition, even if a product candidate qualifies as a breakthrough therapy, the FDA may later decide that the drug no longer meets the conditions for qualification and rescind the Breakthrough Therapy Designation.

We are dependent on our collaboration partners for the successful development of product candidates and, therefore, are subject to the efforts of these partners and our ability to successfully collaborate with these partners.

We have entered into collaboration agreements with Novo Nordisk A/S ("Novo"), F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (together, "Roche"), Eli Lilly and Company ("Lilly"), Alexion Pharmaceuticals, Inc. (together with its affiliates, "Alexion"), Boehringer Ingelheim International GmbH ("BI"), and Alnylam (collectively, our "Collaboration Partners") for the successful development and commercialization of product candidates. The success of our collaborations with our Collaboration Partners and the realization of the milestone and royalty payments under the collaboration agreements depends upon the efforts of our Collaboration Partners, to the extent they are responsible for performance of collaboration activities. Each collaboration partner may not be successful in performance of such activities, including, for example, obtaining approvals for the product candidates developed under the collaboration or in marketing, or arranging for necessary supply, manufacturing, or distribution relationships for, any approved products. Our Collaboration Partners may change their strategic focus or pursue alternative technologies in a manner that results in reduced, delayed, or no additional payments to us under the collaboration agreements. In December 2020, one of our Collaboration Partners, Alexion, entered into a definitive agreement for AstraZeneca to acquire Alexion, which may result in delays and other strategic changes that negatively impact our collaboration with Alexion. Our Collaboration Partners have a variety of marketed products and product candidates under collaboration with other companies, possibly including some of our competitors, and our Collaboration Partners' own corporate objectives may not be consistent with our interests. If our Collaboration Partners fail to develop, obtain regulatory approval for, or ultimately commercialize any product candidate under our collaborations, or if any of our Collaboration Partners terminates their applicable collaboration, our business, financial condition, results of operations, and prospects could be materially and adversely affected. Each of our collaboration agreements is terminable by the applicable collaboration partner any time at will, subject to compliance with applicable notice periods. In addition, if we have a dispute or enter into litigation with any of our Collaboration Partners in the future, it could delay development programs, create uncertainty as to ownership of intellectual property rights, distract management from other business activities, and generate substantial expense.

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

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

If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of preclinical studies or clinical trials, or meet expected deadlines, our clinical development programs could be delayed and otherwise adversely affected. In all events, we are responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the general investigational plan and protocols for the trial as well as applicable laws and regulations. The FDA and certain foreign regulatory authorities, such as the EMA, require preclinical studies to be conducted in accordance with applicable good laboratory practices and clinical trials to be conducted in accordance with applicable FDA regulations and applicable good clinical practices, including requirements for conducting, recording, and reporting the results of preclinical studies and clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of clinical trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. Any such event could have a material adverse effect on our business, financial condition, results of operations, and prospects.

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

We rely on third-party supply and manufacturing companies and organizations to supply the materials, components, and manufacturing services for our research and development, preclinical study, and clinical trial drug supplies. We do not own or lease manufacturing facilities or supply sources for such components and materials; however, we entered into an initial five-year agreement with a supplier for the development, manufacture, and supply of clinical products; this agreement allows for advance preferential

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

Although we have multiple contract manufacturers, two of our amidite manufacturers are based in China, and as a result of the COVID-19 pandemic and an increase in potential political uncertainty, there is an increased risk of technology transfer and supply interruption at those facilities. We have expanded amidite production to the U.S. and currently have greater than 18 months of inventory on hand.

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

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

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, including on account of government-mandated production requirements that our third-party manufacturing partners experience during the COVID-19 pandemic or future public health emergencies, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third party's failure to execute on our manufacturing requirements could adversely affect our business in a number of ways, including:

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

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

From time to time, we may consider strategic transactions, such as collaborations, acquisitions of companies, asset purchases, and out- or in-licensing of product candidates or technologies. In addition to our current collaborations with Novo, Roche, Lilly, Alexion, BI, and Alnylam, we may evaluate and, if strategically attractive, seek to enter into additional collaborations, including with major biopharmaceutical, biotechnology, or pharmaceutical companies. The competition for collaborators is intense, and the negotiation process is time-consuming and complex. Any new collaborations may be on terms that are not optimal for us, and we may

be unable to maintain any existing or future collaborations if, for example, development or approval of a product candidate is delayed, sales of an approved product do not meet expectations, or a collaborator terminates a collaboration. Any such collaborations, or other strategic transactions, may require us to incur non-recurring or other charges, increase our near- and long-term expenditures, and pose significant integration or implementation challenges or disrupt our management or business. These transactions entail numerous operational and financial risks, including exposure to unknown liabilities, disruption of our business, and diversion of our management's time and attention to obtain and 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 impairment charges, increased amortization expenses, difficulty and cost in facilitating the collaboration or combining the operations and personnel of any acquired business, deterioration of relationships with key suppliers, manufacturers, or customers of any acquired business due to changes in management and ownership, and the inability to retain key employees of any acquired business. Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks and have a material adverse effect on our business, results of operations, financial condition, and prospects. Conversely, failure to enter any collaboration or other strategic transaction that would be beneficial to us could delay the development and potential commercialization of our product candidates and have a negative impact on the competitiveness of any product candidate that reaches market.

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

The development and commercialization of drugs is highly competitive. We compete with a variety of multinational pharmaceutical companies and specialized biotechnology companies, as well as technology being developed at universities and other research institutions. Our competitors have developed, are developing, or may develop product candidates and processes competitive with our product candidates, some of which may become commercially available before any of our product candidates. We believe that a significant number of product candidates 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.

Competitive therapeutic treatments include those that have already been approved and accepted by the medical community and any new treatments that enter the market. We are aware of many companies that are working in the field of RNAi therapeutics, including major pharmaceutical companies and a number of biopharmaceutical companies such as Alnylam, Arrowhead Pharmaceuticals, Inc., Arbutus Biopharma Corporation, Silence Therapeutics plc, Quark Pharmaceuticals, Inc., and Novartis International AG.

We also compete with companies working to develop antisense and other RNA-based drugs including Ionis Pharmaceuticals, Moderna, Inc., Acuitas Therapeutics, and Wave Life Sciences Ltd. Like RNAi therapeutics, antisense drugs target mRNA with the objective of suppressing the activity of specific genes. The development of antisense drugs is more advanced than that of RNAi therapeutics with several antisense therapies currently approved, and antisense technology may become the preferred technology for products that target mRNAs.

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

Beyond RNA-based platform competition, there are a number of potential competitors working to develop therapeutics in our areas of research, including Oxthera AB, Allena Pharmaceuticals, Inc., Vertex Pharmaceuticals, Inc., Assembly Biosciences, Inc., Gilead Sciences, Inc., GlaxoSmithKline plc, Vir Biotechnology, Inc., Beam Therapeutics Inc., Intellia Therapeutics, Inc., Apic Bio, Inc., Biocodex, S.A., and Adial Pharmaceuticals, Inc.

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

Interim and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available or as additional analyses are conducted and as the data are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim or preliminary data from our clinical studies. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Material adverse changes between preliminary or interim data and final data could significantly harm our business prospects.

As more of our product candidates advance into clinical trials, including pivotal trials, and commercialization, if approved, we may experience difficulties in managing our growth and expanding our operations.

Thus far, we have only advanced nedosiran, RG6346, and belcesiran into clinical development. As a result, compared to larger pharmaceutical companies, we have relatively limited experience as a company in drug development and with clinical trials of product candidates, including pivotal trials. As our product candidates enter and advance through preclinical studies and clinical trials, including pivotal trials, we will need to expand our development, regulatory, manufacturing, and commercialization capabilities or contract with other organizations to provide these capabilities for us or otherwise partner with other companies for the advancement or commercialization, if approved, of such product candidates. In the future, as our product candidates progress in development, we expect to have to manage additional relationships with collaborators, CROs, clinical trial sites, investigators, suppliers, and other firms. 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.

We or our collaborative partners may conduct clinical trials for product candidates outside of the U.S., and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We or our collaborative partners may in the future choose to conduct one or more clinical trials outside the U.S., including in Europe. For instance, our clinical trials of nedosiran, RG6346, and belcesiran each include subjects outside of the U.S. The acceptance of study data from clinical trials conducted outside of the U.S. or another jurisdiction by the FDA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the U.S., the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to Good Clinical Practices ("GCP") regulations; and (iii) the data may be considered valid without the need for an ongoing site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the U.S. or the applicable international jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be

costly and time-consuming and delay aspects of our business plan, and which may result in product candidates that we may develop not receiving approval or clearance for commercialization in the applicable jurisdiction.

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, if at all, we will be unable to successfully commercialize any such future products.

We initially planned to commercialize nedosiran in the U.S. ourselves, if approved, and looked to partner with a third party to commercialize nedosiran outside of the U.S. However, based on the inconsistent results observed in the PH2 subtype of patients included in our PHYOX2 pivotal study, we now plan to pursue commercial out-licensing opportunities to commercialize nedosiran in major markets including the U.S., subject to approvals. Even if our NDA for nedosiran receives marketing approvals, we may not be successful in commercializing nedosiran through third parties, in which case, our business, financial condition, results of operations, and prospects could be materially and adversely affected.

As a company, we have no near-term plan to establish our own fully integrated commercial operations in the U.S. or in other markets. As a result, even if any of our product candidates are approved, in the near-term Dicerna would require a collaboration partner or partners to commercialize such product candidates, which would necessitate our having to enter into collaboration agreements with third parties to perform these services on acceptable terms, if at all. In the future, if we decide to market any such approved products directly, we will need to commit significant financial, legal, and managerial resources to develop a marketing and sales force with technical expertise and supporting distribution, administration, and compliance capabilities. If we rely on third parties with such capabilities to market for any such approved products, we will need to establish and maintain marketing and distribution arrangements with third parties, and there can be no assurance that we will be able to enter into such arrangements on acceptable, compliant terms, or at all. In entering into third-party marketing or distribution arrangements, any commercial 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 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.

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

Even if we receive marketing and commercialization approval of a product candidate, we and our third-party service providers will be subject to continuing regulatory requirements, including a broad array of regulations related to establishment registration and product listing, manufacturing processes, risk management measures, quality and pharmacovigilance systems, post-approval clinical studies, labeling, advertising and promotional activities, record keeping, distribution, adverse event reporting, import and export of pharmaceutical products, pricing, sales and marketing, and fraud and abuse requirements. We are required to submit safety and other post-market information and reports and are subject to continuing regulatory review, including in relation to adverse patient experiences with the product and clinical results that are reported after a product is made commercially available, both in the U.S. and any foreign jurisdiction in which we seek regulatory approval. The FDA and certain foreign regulatory authorities, such as the EMA, have significant post-market authority, including the authority to require labeling changes based on new safety information and to require post-market studies or clinical trials to evaluate safety risks related to the use of a product or to require withdrawal of the product from the market. The FDA also has the authority to require a risk evaluation and mitigation strategy (“REMS”) plan after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug. The EMA now routinely requires risk management plans (“RMPs”) as part of the marketing authorization application process, and such plans must be continually modified and updated throughout the lifetime of the product as new information becomes available. In addition, for nationally authorized medicinal products, the relevant governmental authority of any EU Member State can request an RMP whenever there is a concern about a risk affecting the benefit risk balance of the product. The manufacturer and manufacturing facilities we use to make a future product, if any, will also be subject to periodic review and inspection by the FDA and other regulatory agencies, including for continued compliance with cGMP requirements. The discovery of any new or previously unknown problems with our third-party manufacturers, manufacturing processes, or facilities may result in restrictions on the product, manufacturer, or facility, including withdrawal of the product from the market. If we rely on third-party manufacturers, we will only have limited control over compliance with applicable rules and regulations by such manufacturers. Any product promotion and advertising will also be subject to regulatory requirements and continuing regulatory review. If we or our collaborators, manufacturers, or service providers fail to comply with applicable continuing regulatory requirements in the U.S. or foreign jurisdictions in which we seek to market our products, we or they may be subject to, among other things, fines, warning and untitled letters, clinical holds, delay or refusal by the FDA or foreign regulatory authorities to approve pending applications or supplements to approved applications, suspension, refusal to renew or withdrawal of regulatory approval, product recalls, seizures or administrative detention of products, refusal to permit the import or export of products, operating restrictions, inability to participate in government programs including Medicare and Medicaid,

and total or partial suspension of production or distribution, injunction, restitution, disgorgement, debarment, civil penalties, and criminal prosecution.

We face risks arising from the results of the public referendum held in the United Kingdom and its subsequent withdrawal from the European Union.

On June 23, 2016, the United Kingdom ("UK") held a referendum in which a majority of the eligible members of the electorate voted to leave the EU. The UK's withdrawal from the EU is commonly referred to as Brexit. Pursuant to Article 50 of the Treaty on European Union, the UK ceased being a Member State of the EU on January 31, 2020. A transition period began February 1, 2020 and continued until December 31, 2020, during which EU laws remained applicable to the UK. In December 2020, the UK and the EU agreed on a trade and cooperation agreement ("TCA"), which became provisionally applicable on January 1, 2021 and has been formally applicable since May 1, 2021, under which the EU and the UK will now form two separate markets governed by two distinct regulatory and legal regimes. The TCA covers the general objectives and framework of the relationship between the UK and EU, including as it relates to trade, transport, and visas. The TCA also includes limited specific provisions concerning pharmaceuticals, which include the mutual recognition of Good Manufacturing Practice ("GMP"), inspections of manufacturing facilities for medicinal products, and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations. Depending on the application of the terms of the TCA and the extent to which UK regulations diverge from EU regulations, we could face new regulatory costs and challenges. Many effects of Brexit are also still uncertain, for example with respect to certain financial laws and regulations. This lack of clarity on future UK laws and regulations and their interaction with EU laws and regulations may negatively impact foreign direct investment in the UK, increase costs, depress economic activity, and restrict access to capital. The uncertainty concerning the UK's long-term legal, political, and economic relationship with the EU after Brexit may be a source of instability in the international markets, create significant currency fluctuations, and/or otherwise adversely affect trading agreements or similar cross-border co-operation arrangements (whether economic, tax, fiscal, legal, regulatory, or otherwise) beyond the date of Brexit. We have a subsidiary located in the UK, which we established to allow us to conduct clinical trials in EU Member States. While we have begun to transition our subsidiaries in Ireland and in Germany to support activities in the EU, there can be no assurance that we will not experience disruptions or other operational challenges in connection with such transition.

These developments may have a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and limit the ability of key market participants to operate in certain financial markets. In particular, it could also lead to a period of considerable uncertainty in relation to the UK financial and banking markets, as well as on the regulatory process in Europe. Asset valuations, currency exchange rates, and credit ratings may also be subject to increased market volatility.

In addition, if other EU Member States pursue withdrawal, barrier-free access between the other EU Member States or among the European Economic Area ("EEA") overall could be diminished or eliminated. The long-term effects of Brexit will depend on how the terms of the TCA take effect in practice and on any further agreements (or lack thereof) between the UK and the EU.

Such a withdrawal from the EU is unprecedented, and it is unclear how the restrictions on the UK's access to the European single market for goods, capital, services, and labor within the EU, or single market, and the wider commercial, legal, and regulatory environment, will impact our current and future operations (including business activities conducted by third parties and contract manufacturers on our behalf) and clinical activities in the UK in the long term. In addition to the foregoing, our UK operations support our current and future operations and clinical activities in other countries in the EU and the EEA, and these operations and clinical activities could be disrupted by Brexit.

We may also face new regulatory costs and challenges that could have an adverse effect on our operations. Now that the UK has left the EU, the UK will lose the benefits of global trade agreements negotiated by the EU on behalf of its members, which may result in increased trade barriers that could make our doing business in the EU and the EEA more difficult. Furthermore, Great Britain will now no longer be covered by the centralized procedures for obtaining EEA-wide marketing and manufacturing authorizations from the EMA (under the Northern Irish Protocol, centralized marketing authorizations will continue to be recognized in Northern Ireland) and a separate process for authorization of drug products will be required in Great Britain, resulting in an authorization covering the UK or Great Britain only. Brexit has created economic uncertainty surrounding the terms of Brexit and its consequences could adversely impact customer confidence resulting in customers reducing their spending budgets on our solutions, which could adversely affect our business, revenue, financial condition, results of operations, and could adversely affect the market price of our common shares.

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

In some countries, particularly Member States of the EU, the pricing of prescription drugs may be subject to governmental control, at national as well as at regional levels. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a product. In addition, in the U.S. and elsewhere, there can be considerable

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

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

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

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

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

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

Despite the implementation of security measures, our internal computer systems and those of third parties with which we do business, including our CROs and other contractors and consultants, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication and electrical failures. Such events, as well as power outages, natural disasters (including extreme weather), terrorist attacks, phishing or ransomware attacks, or other similar events, could cause interruptions of our operations.

In the ordinary course of our business, we collect and store sensitive data, including, among other things, legally protected patient health information, personally identifiable information about our employees, intellectual property, and proprietary business information. We manage and maintain our applications and data utilizing on-site systems and outsourced vendors. These applications and data encompass a wide variety of business-critical information, including research and development information, commercial information, and business and financial information. Because information systems, networks, and other technologies are critical to many of our operating activities, shutdowns or service disruptions at our company or vendors that provide information systems, networks, or other services to us pose increasing risks. Such disruptions may be caused by events such as computer hacking, phishing attacks, ransomware, dissemination of computer viruses, worms, and other destructive or disruptive software, denial of service attacks and other malicious activity, as well as power outages, natural disasters (including extreme weather), terrorist attacks, or other similar events. Such events could have an adverse impact on us and our business, including loss of data and damage to equipment and data. In addition, system redundancy may be ineffective or inadequate, and our disaster recovery planning may not be sufficient to cover all eventualities. Significant events could result in a disruption of our operations, damage to our reputation, or a loss of revenues. In addition, we may not have adequate insurance coverage to compensate for any losses associated with such events. 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.

We could be subject to risks caused by misappropriation, misuse, leakage, falsification, or intentional or accidental release or loss of information maintained in the information systems and networks of our company and our vendors, including personal information of our employees and patients, and company and vendor confidential data. In addition, outside parties may attempt to penetrate our systems or those of our vendors or fraudulently induce our personnel or the personnel of our vendors to disclose sensitive information to gain access to our data and/or systems. We may experience threats to our data and systems, including malicious codes and viruses, phishing, and other cyber-attacks. The number and complexity of these threats continue to increase over time. If a material breach of our information technology systems or those of our vendors occurs, the market perception of its effectiveness of our security measures could be harmed and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. Certain data breaches must also be reported to affected individuals and the government, and in some cases to the media, under provisions of the U.S. federal Health Insurance Portability and Accountability Act (“HIPAA”), as amended by the Health Information Technology for Economic and Clinical Health Act (“HITECH”), other U.S. federal and state law, and requirements of non-U.S. jurisdictions, including the General Data Protection Regulation (“GDPR”), and financial penalties may also apply. To the extent that any disruption or security breach were to result in a loss of, or damage to, internal computer systems, or those used by our CROs or other independent organizations, advisors, contractors or consultants, our data, or inappropriate disclosure of confidential or proprietary information of the Company or patients, we could incur liability, reputational harm, and the development of our product candidates could be delayed.

In addition, we could be subject to regulatory actions and/or claims made by individuals and groups in private litigation involving privacy issues related to data collection and use practices and other data privacy laws and regulations, including claims for misuse or inappropriate disclosure of data, as well as unfair or deceptive practices. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls, and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become increasingly sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely. As we outsource more of our information systems to vendors, engage in more electronic transactions with payors and patients, and rely more on cloud-based information systems, the related security risks will increase and we may need to expend additional resources to protect our technology and information systems. In addition, there can be no assurance that our internal information technology systems or those of our third-party contractors, or our consultants’ efforts to implement adequate security and control measures, will be sufficient to protect us against breakdowns, service disruption, data deterioration, or loss in the event of a system malfunction, or prevent data from being stolen or corrupted in the event of a cyberattack, security breach, industrial espionage attacks, or insider threat attacks which could result in financial, legal, business, or reputational harm.

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

Our research, development, and manufacturing involve the use of hazardous materials and various chemicals. We maintain quantities of various flammable and toxic chemicals in one of our facilities in Lexington, Massachusetts, that are required for our research, development, and manufacturing activities, as applicable. 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 Lexington facility comply with the relevant guidelines of Lexington, 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.

Despite the use of cloud-based information storage systems and services for certain key corporate information, our internal information technology and other infrastructure systems, including corporate firewalls, servers, leased lines, and connection to the Internet, face the risk of systemic failure that could disrupt our operations. A significant disruption in the availability of our information technology and other internal infrastructure systems could cause interruptions in our collaborations and delays in our research and development work. While we qualify and seek to ensure all information technology systems and services that we utilize have appropriate cybersecurity and operations controls, we are dependent on third parties to ensure their operations meet our information technology requirements.

Our current operations are largely concentrated in our locations in Lexington, Massachusetts and any events affecting these locations may have material adverse consequences.

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

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

We have incurred substantial losses during our history, and may never achieve profitability or, if we do, such profitability may not be sustained. 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 taxable 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 performed an analysis on whether we have experienced any ownership changes in the past. Our analysis indicates that we experienced ownership changes in November 2007, October 2010, February 2014, and March 2018. Our net operating losses are subject to such limitation. As of June 30, 2021, we continue to have significant U.S. federal and state level net operating loss carryforwards that could be reduced or lost if we experience any further ownership changes, which could have an adverse effect on our business, financial position, results of operations, and prospects.

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

As of June 30, 2021, we had $709.6 million in cash, cash equivalents, and held-to-maturity investments. We historically have invested substantially all of our available cash and cash equivalents in corporate bonds, commercial paper, securities issued by the U.S. government, certificates of deposit, and money market funds meeting the criteria of our investment policy, which is focused on the preservation of our capital. These investments are subject to general credit, liquidity, market, and interest rate risks. For example, the impact of U.S. sub-prime mortgage defaults in recent years affected various sectors of the financial markets and caused credit and liquidity issues. We may realize losses in the fair value of these investments or a complete loss of these investments, which would have a negative effect on our consolidated financial statements.

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

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

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

Risks Related to Intellectual Property

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

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

As of June 30, 2021, our worldwide patent estate, not including the patents and patent applications that we have licensed from third parties, included more than 105 issued patents or allowed patent applications and over 380 pending patent applications supporting commercial development of our RNAi molecules and delivery technologies. We may not be able to apply for patents on certain aspects of our product candidates or delivery technologies in a timely fashion or at all. Our existing issued and granted patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing products and technology. There is no guarantee that any of our pending patent applications will result in issued or granted patents, that any of our issued or granted patents will not later be found to be invalid or unenforceable, or that any issued or granted patents will include claims that are sufficiently broad to cover our product candidates or delivery technologies or to provide meaningful protection from our competitors. Moreover, the patent position of biotechnology and pharmaceutical companies can be highly uncertain because it involves complex legal and factual questions that may be tested in multiple jurisdictions globally. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our current and future proprietary technology and product candidates are covered by valid and enforceable patents or are effectively maintained as trade secrets. If third parties disclose or misappropriate our proprietary rights, it may materially and adversely impact our position in the market.

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

In addition, there are numerous recent changes to the patent laws and proposed changes to the rules of the USPTO which may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. The U.S. Supreme Court has ruled on several patent cases in recent years, some of which either narrow the scope of patent protection available in certain circumstances or weaken the rights of patent owners in certain situations. The 2013 decision by the U.S. Supreme Court in Association for Molecular Pathology v. Myriad Genetics, Inc. precludes a claim to a nucleic acid having a stated nucleotide sequence which is identical to a sequence found in nature and unmodified. We currently are not aware of an immediate impact of this decision on our patents or patent applications because we are developing nucleic acid products that are not found in nature. However, this decision has yet to be fully interpreted by courts and by the USPTO. We cannot assure you that the interpretations of this decision or subsequent rulings will not adversely impact our patents or patent applications. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing U.S. patents

could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

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

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

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

Research and development of RNAi-based therapeutics and other oligonucleotide-based therapeutics has resulted in many patents and patent applications from organizations and individuals seeking to obtain patent protection in the field. Our efforts are based on RNAi technology that we have licensed and that we have developed internally and own or co-own. We have chosen this approach to increase our likelihood of technical success and our freedom to operate. We have obtained grants and issuances of RNAi-based patents and have licensed other patents from third parties on exclusive and non-exclusive bases. The issued patents and pending patent applications in the U.S. and in key markets around the world that we own, co-own, or license claim many different methods, compositions, and processes relating to the discovery, development, manufacture, and commercialization of RNAi therapeutics. Specifically, we own, co-own, or have licensed a portfolio of patents, patent applications, and other intellectual property covering: (1) certain aspects of the structure and uses of RNAi molecules, including their manufacture and use as therapeutics, and RNAi-related mechanisms, (2) chemical modifications to RNAi molecules that improve their properties and suitability for therapeutic uses, (3) RNAi molecules directed to specific gene sequences and drug targets as treatments for particular diseases, and (4) delivery technologies, such as in the field of lipid nanoparticles and lipid nanoparticle formulation, and chemical modifications such as conjugation to targeting moieties.

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

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

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

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

We may 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 may, in the future, rely on intellectual property rights licensed from third parties to protect our technology, including licenses that give us rights to third-party intellectual property that is necessary or useful for our business. We also may license additional third-party intellectual property in the future. Our success may 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, such patents may have claim breadth coverage insufficient to protect our interests, may determine not to pursue litigation against other companies that are infringing these patents, or may pursue litigation less aggressively than we would. Further, we may not obtain exclusive rights, which would allow for third parties to develop competing products. Without protection for, or exclusive right to, the intellectual property we license, other companies might be able to offer substantially identical products for sale, which could adversely affect our competitive business position and harm our business prospects. In addition, we sublicense certain of our rights under our third-party licenses to BI and Alnylam and may sublicense such rights to current or future collaborators. Any impairment of these sublicensed rights could result in reduced revenue under our collaboration agreements with BI and Alnylam or result in termination of an agreement by one or more of our existing or any other future collaborators.

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

Obtaining a valid and enforceable issued or granted patent covering our technology in the U.S. and worldwide can be extremely costly. In jurisdictions where we have not obtained patent protection, competitors may use our technology to develop their own products, and further, may export otherwise infringing products to territories where we have patent protection, but where it is more difficult to enforce a patent compared to the U.S. We also may face competition in jurisdictions where we do not have issued or

granted patents or where our issued or granted patent claims or other intellectual property rights are not sufficient to prevent competitor activities in these jurisdictions. The legal systems of certain countries, particularly certain developing countries, make it difficult to enforce patents and such countries may not recognize other types of intellectual property protection, particularly that relating to biopharmaceuticals. This could make it difficult for us to prevent the infringement of our patents or marketing of competing products in violation of our proprietary rights generally in certain jurisdictions. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

We generally file a provisional patent application first (a priority filing) at the USPTO. A U.S. utility application and/or international application under the Patent Cooperation Treaty ("PCT") are usually filed within 12 months after the priority filing. Based on the PCT filing, national and regional patent applications may be filed in the EU, Japan, Australia, and Canada and, depending on the individual case, also in any or all of, inter alia, China, India, South Korea, Singapore, Taiwan, and South Africa. We have so far not filed for patent protection in all national and regional jurisdictions where such protection may be available. In addition, we may decide to abandon national and regional patent applications before grant. Finally, the grant proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications might be refused in some jurisdictions, while granted by others. Depending on the country, various scopes of patent protection may be granted on the same product candidate or technology.

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

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

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

If we were to initiate legal proceedings against a third party to enforce a patent covering one of our products or our technology, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during patent prosecution. The outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during patent prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on

one or more of our products or certain aspects of our platform technology. Such a loss of patent protection could have a material adverse impact on our business. Patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without legally infringing our patents or other intellectual property rights.

If we or our collaborative partners 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.

Any future licenses we enter are likely to impose various development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement, and other obligations on us or certain of our collaborative partners that receive sublicenses. If we breach any of these obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages, and the licensor may have the right to terminate the license, which could result in us being unable to develop, manufacture, and sell products that are covered by the licensed technology, or enable a competitor to gain access to the licensed technology. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

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

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

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

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

Many of our employees were previously employed at universities or biotechnology or pharmaceutical companies, including our competitors or potential competitors. From time to time, we have received correspondence from other companies alleging the improper use or disclosure, or inquiring regarding the use or disclosure, by certain of our employees who have previously been employed elsewhere in our industry, including with our competitors, of their former employer's trade secrets or other proprietary information. Responding to these allegations can be costly and disruptive to our business, even when the allegations are without merit, and can be a distraction to management.

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

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

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

Risks Related to Government Regulation

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

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

We have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA as well as foreign regulatory authorities, such as the EMA. The time required to obtain FDA and foreign regulatory approvals is unpredictable but typically takes many years following the commencement of clinical trials, depending upon the type, complexity, and novelty of the product candidate. The standards that the FDA and its foreign counterparts use when regulating us are not always applied predictably or uniformly and can change. Any analysis we perform of data from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit, or prevent regulatory approval. We may also encounter unexpected delays or increased costs due to new government regulations, for example, from future legislation or administrative action, or from changes in the policy of the FDA or foreign regulatory authorities during the period of product development, clinical trials, and regulatory review by the FDA or foreign regulatory authorities. It is impossible to predict whether legislative changes will be enacted, or whether FDA or foreign laws, regulations, guidance, or interpretations will be changed, or what the impact of such changes, if any, may be.

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

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

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

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

marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include, but are not limited to, the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering, or providing remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for a healthcare item or service, or the purchasing or ordering of an item or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare or Medicaid. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers, and formulary managers, among others, on the other. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, individual imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act or federal civil money penalties;
- the federal civil and criminal false claims laws and civil monetary penalty laws, such as the U.S. federal False Claims Act ("FCA"), which imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities (including manufacturers) for, among other things, knowingly presenting or causing to be presented, to the federal government, claims for payment that are false or fraudulent, making, using, or causing to be made or used, a false statement or record material to payment of a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding, decreasing, or concealing an obligation to pay money to the federal government. The government may deem manufacturers to have "caused" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customer or promoting a product off-label. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA;
- HIPAA includes a fraud and abuse provision which imposes criminal and civil liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program (including private payors), or knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items, or services, regardless of the payor (e.g., public or private). Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;
- HIPAA, as amended by HITECH, and its implementing regulations, which impose obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses, as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information, and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;
- federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- the federal false statements statute which prohibits knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items, or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;
- the federal Physician Payment Sunshine Act created under the Affordable Care Act ("ACA"), and its implementing regulations which require that manufacturers of drugs, biologicals, devices, and medical supplies for which payment is available under Medicare, Medicaid, and Children's Health Insurance Program (with certain exceptions) report annually to the Department of Health and Human Services information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners;
- federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs;

- The Foreign Corrupt Practices Act prohibits companies and their intermediaries from making, or offering or promising to make, improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;
- the EU General Data Protection Regulation (EU) 2016/679, which introduced new data protection requirements in the EU, as well as substantial fines for breaches of the data protection rules as of May 25, 2018. The GDPR enhances data protection obligations for processors and controllers of personal data, including, for example, expanded disclosures about how personal information is to be used, limitations on retention of information, mandatory data breach notification requirements, and onerous new obligations on services providers. Non-compliance with the GDPR may result in monetary penalties of up to €20 million or 4% of worldwide revenue, whichever is higher (note that non-compliance with the UK GDPR may result in monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher). The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of personal data, such as healthcare data or other sensitive information, could greatly increase our cost of providing our products and services or even prevent us from offering certain services in jurisdictions in which we operate;
- the California Consumer Privacy Act ("CCPA"), which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA requires covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt out of certain sales or transfers of personal information. The CCPA went into effect on January 1, 2020, and the California Attorney General commenced enforcement actions against violators on July 1, 2020. While there are currently exceptions for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may impact our business activities; and
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

Additionally, we may be subject to analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws potentially applicable to sales or marketing arrangements and claims involving healthcare items or services reimbursed by nongovernmental third-party payors, including private insurers. Further, certain state laws require pharmaceutical manufacturers to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, and may require pharmaceutical manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures. There may also be additional state laws that apply to our business which govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. The approval and commercialization of any of our drug candidates outside the U.S. will also likely subject us to non-U.S. equivalents of the healthcare laws mentioned above, among other non-U.S. laws.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions, and settlements in the healthcare industry. Responding to investigations can be time- and resource-consuming and can divert management's attention from the business. Any such investigation or settlement could increase our costs or otherwise have an adverse effect on our business.

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

If we or current or future collaborators, manufacturers, or service providers fail to comply with applicable federal, state, or foreign laws or regulations, we could be subject to enforcement actions, which could affect our ability to develop, market, and sell our products successfully and could harm our reputation and lead to reduced acceptance of our products by the market. These enforcement actions include, among others:

- adverse regulatory inspection findings;

- warning or untitled letters;
- voluntary or mandatory product recalls or public notification or medical product safety alerts to healthcare professionals;
- restrictions on, or prohibitions against, marketing our products;
- restrictions on, or prohibitions against, importation or exportation of our products;
- suspension of review or refusal to approve pending applications or supplements to approved applications, including due to pending enforcement actions or a finding of an enforcement action;
- exclusion from participation in government-funded healthcare programs;
- exclusion from eligibility for the award of government contracts for our products;
- a corporate integrity agreement;
- FDA debarment of individuals at our Company;
- suspension or withdrawal of product approvals;
- seizure or administrative detention of products;
- injunctions; and
- civil and criminal penalties and fines.

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

The regulations that govern marketing approvals, pricing, coverage, and reimbursement for new drugs vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. Although we intend to monitor these regulations, our programs are currently in the early stages of development and we will not be able accurately 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.

In the U.S. and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors, is critical to new product acceptance. Our ability to commercialize any products successfully will also depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. The availability of coverage and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments. Sales of products that we may identify will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. However, there may be significant delays in obtaining coverage for newly approved drugs. Moreover, eligibility for coverage does not necessarily signify that a drug will be reimbursed in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution costs. Also, interim payments for new drugs, if applicable, may be insufficient to cover our costs and may not be made permanent. Thus, even if we succeed in bringing one or more products to the market, these products may not be considered medically necessary or cost-effective, and the amount reimbursed for any products may be insufficient to allow us to sell our products on a competitive basis. Because our programs are in the early stages of development, we are unable at this time to determine their cost effectiveness, or the likely level or method of reimbursement. In addition, obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical, and cost-effectiveness data for the use of our product on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize any product candidate that we successfully develop.

Increasingly, the third-party payors who reimburse patients or healthcare providers, such as government and private insurance plans, are seeking greater upfront discounts, additional rebates, and other concessions to reduce the prices for pharmaceutical products. Factors payors consider in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

If the price we are able to charge for any products we develop is insufficient to cover our costs or provide an acceptable margin, our product candidates are not considered medically necessary or cost effective, or the reimbursement provided for such products is inadequate in light of our development and other costs, our return on investment could be adversely affected.

We currently expect that certain drugs we develop may need to be administered under the supervision of a physician on an outpatient basis. Under currently applicable U.S. law, certain drugs that are not usually self-administered (including injectable drugs) may be eligible for coverage under Medicare through Medicare Part B. Specifically, Medicare Part B coverage may be available for eligible beneficiaries when the following, among other requirements have been satisfied:

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

Average prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S. Reimbursement rates under Medicare Part B would depend in part on whether the newly approved product would be eligible for a unique billing code. Self-administered, outpatient drugs are typically reimbursed under Medicare Part D, and drugs that are administered in an inpatient hospital setting are typically reimbursed under Medicare Part A under a bundled payment. It is difficult for us to predict how Medicare coverage and reimbursement policies will be applied to our products in the future and coverage and reimbursement under different federal healthcare programs are not always consistent. Medicare reimbursement rates may also reflect budgetary constraints placed on the Medicare program.

Commercial third-party payors often rely upon Medicare coverage policies and payment limitations in setting their own reimbursement rates. These coverage policies and limitations may rely, in part, on compendia listings for approved therapeutics. Our inability to promptly obtain relevant compendia listings, coverage, and adequate reimbursement from both government-funded and private payors for new drugs that we develop and for which we obtain regulatory approval could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products, and our financial condition. Further, due to the COVID-19 pandemic, millions of individuals have lost or will be losing employer-based insurance coverage, which may adversely affect our ability to commercialize our product candidates even if there is adequate coverage and reimbursement from third-party payors.

We expect that these and other healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and lower reimbursement and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs once marketing approval is obtained.

In addition, there has been increasing legislative and enforcement interest in the U.S. with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient assistance programs, and reform government program reimbursement methodologies for drugs. For example, at the federal level, President Biden signed an Executive Order on July 9, 2021 affirming the administration’s policy to (i) support legislative reforms that would lower the prices of prescription drug and biologics, including by allowing Medicare to negotiate drug prices, by imposing inflation caps, and by supporting the development and market entry of lower-cost generic drugs and biosimilars;

and (ii) support the enactment of a public health insurance option. Among other things, the Executive Order also directs the Department of Health and Human Services ("HHS") to provide a report on actions to combat excessive pricing of prescription drugs, enhance the domestic drug supply chain, reduce the price that the Federal government pays for drugs, and address price gouging in the industry; and directs the FDA to work with states and Indian Tribes that propose to develop section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 and the FDA's implementing regulations. The FDA released such implementing regulations on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, CMS issued an Interim Final Rule implementing the Most Favored Nation ("MFN") Model under which Medicare Part B reimbursement rates will be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. The MFN Model regulations mandate participation by identified Part B providers and would have applied to all U.S. states and territories for a seven-year period beginning January 1, 2021, and ending December 31, 2027. The MFN is currently subject to ongoing litigation. Further, authorities in Canada have passed rules designed to safeguard the Canadian drug supply from shortages. If implemented, importation of drugs from Canada and the MFN Model may materially and adversely affect the price we receive for any of our product candidates. Additionally, on December 2, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point of sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. On December 2, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point of sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Further, implementation of this change and new safe harbors for point-of-sale reductions in price for prescription pharmaceutical products and pharmacy benefit manager service fees are currently under review by the Biden administration and may be amended or repealed. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

HHS has already implemented certain of these measures while others are pending. For example, in May 2019, the Centers for Medicare and Medicaid Services, or CMS, issued a final rule to allow Medicare Advantage Plans the option of using step therapy, a type of prior authorization, for Part B drugs beginning January 1, 2020. Although a number of these and other proposed measures will require authorization through additional legislation to become effective, it is unclear whether the Biden administration will challenge, reverse, revoke, or otherwise modify these recent executive and administrative actions. Individual states in the U.S. have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We believe that the efforts of governments and other third-party payors to contain or reduce the cost of healthcare and legislative and regulatory proposals to broaden the availability of healthcare will continue to affect the business and financial condition of pharmaceutical and biopharmaceutical companies. A number of legislative and regulatory changes in the healthcare system in the U.S. and other major healthcare markets have been proposed, and such efforts have expanded substantially in recent years. These developments could, directly or indirectly, affect our ability to sell our products, if approved, at a favorable price.

In 2010, the U.S. Congress passed the ACA, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of health spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry, and impose additional policy reforms. Since then, the ACA has undergone executive, judicial, and legislative challenges, and while the Biden administration has signaled an intent to bolster the ACA, ongoing uncertainty around the future of the ACA and, in particular, the impact to reimbursement levels, may lead to uncertainty or delay in the purchasing decisions of our customers, which may in turn negatively impact our product sales. If there are not adequate reimbursement levels, our business and results of operations could be adversely affected.

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

- increases to pharmaceutical manufacturer rebate liability under the Medicaid Drug Rebate Program due to an increase in the minimum basic Medicaid rebate on most branded prescription drugs and the application of Medicaid rebate liability to drugs used in risk-based Medicaid managed care plans;
- a Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% (increased pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point-of-sale discounts off negotiated prices of applicable brand

drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;

- the expansion of the 340B Drug Pricing Program to require discounts for "covered outpatient drugs" sold to certain children's hospitals, critical access hospitals, freestanding cancer hospitals, rural referral centers, and sole community hospitals;
- requirements imposed on pharmaceutical companies to offer discounts on brand-name drugs to patients who fall within the Medicare Part D coverage gap, commonly referred to as the "Donut Hole";
- requirements imposed on pharmaceutical companies to pay an annual non-tax-deductible fee to the federal government based on each company's market share of prior year total sales of branded drugs to certain federal healthcare programs, such as Medicare, Medicaid, Department of Veterans Affairs, and Department of Defense. Since we currently expect our branded pharmaceutical sales to constitute a small portion of the total federal healthcare program pharmaceutical market, we do not currently expect this annual assessment to have a material impact on our financial condition; and
- for products classified as biologics, marketing approval for a follow-on biologic product may not become effective until 12 years after the date on which the reference innovator biologic product was first licensed by the FDA, with a possible six-month extension for pediatric products. After this exclusivity ends, it may be possible for biosimilar manufacturers to enter the market, which is likely to reduce the pricing for the innovator product and could affect our profitability if our products are classified as biologics.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect that there will be additional challenges and amendments to the ACA in the future. The previous administration issued various Executive Orders which eliminated cost sharing subsidies and various provisions that would impose a fiscal burden on states or a cost, fee, tax, penalty, or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices; and Congress has introduced several pieces of legislation aimed at significantly revising or repealing the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for the purpose of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including, among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures of the Biden administration or other efforts, if any, to challenge, repeal, or replace the ACA will impact our business.

Also, in 2018, the Trickett Wendler, Frank Mogiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017 provided a federal framework for certain patients with life-threatening diseases to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

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

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

U.S. federal government agencies currently face potentially significant spending reductions. The Budget Control Act of 2011 (the "BCA") established a Joint Select Committee on Deficit Reduction, which was tasked with achieving a reduction in the federal debt level of at least $1.2 trillion. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction for fiscal years 2012 through 2021, triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect beginning on April 1, 2013 and will stay in effect through 2030 unless additional Congressional action is taken. Pursuant to the CARES Act and subsequent legislation, these reductions have been suspended from May 1, 2020 through December 31, 2021 due to the COVID-19 pandemic.

More recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which have resulted in several recent Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform

government program reimbursement methodologies for pharmaceutical products. Individual states in the U.S. have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. On July 24, 2020 and September 13, 2020, former President Trump announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. As a result, on November 20, 2020, CMS issued an Interim Final Rule implementing the Most Favored Nation ("MFN") Model under which Medicare Part B reimbursement rates will be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. The MFN Model regulations mandate participation by identified Part B providers and will apply in all U.S. states and territories for a seven-year period beginning January 1, 2021 and ending December 31, 2027. On December 28, 2020, a judge in the U.S. District Court for the Northern District of California granted a preliminary injunction prohibiting CMS from implementing the MFN rule pending completion of the comment and rulemaking process required under the Administrative Procedures Act. On January 13, 2021, in a separate lawsuit brought by industry groups in the U.S. District of Maryland, the government defendants entered a joint motion to stay litigation on the condition that the government would not appeal the preliminary injunction granted in the U.S. District Court for the Northern District of California and that performance for any final regulation stemming from the MFN Interim Final Rule shall not commence earlier than 60 days after publication of that regulation in the Federal Register. Further, authorities in Canada have passed rules designed to safeguard the Canadian drug supply from shortages. If implemented, importation of drugs from Canada and the MFN Model may materially and adversely affect the price we receive for any of our product candidates. We will continue to monitor the impact this rule and subsequent challenges may have on our business.

Additionally, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to an order entered by the U.S. District Court for the District of Columbia, the portion of the rule eliminating safe harbor protection for certain rebates related to the sale or purchase of a pharmaceutical product from a manufacturer to a plan sponsor under Medicare Part D has been delayed to January 1, 2023. Further, implementation of this change and new safe harbors for point-of-sale reductions in price for prescription pharmaceutical products and pharmacy benefit manager service fees are currently under review by the Biden administration and may be amended or repealed.

The full impact on our business of any future cuts in Medicare or other programs is uncertain. In addition, we cannot predict any impact the U.S. President's administration and the U.S. Congress may have on the federal budget. If federal spending is reduced, anticipated budgetary shortfalls may also impact the ability of relevant agencies, such as the FDA or the National Institutes of Health, to continue to function at current levels. Amounts allocated to federal grants and contracts may be reduced or eliminated. These reductions may also impact the ability of relevant agencies to timely review and approve drug research and development, manufacturing, and marketing activities, which may delay our ability to develop, market, and sell any products we may develop.

Recent federal legislation and actions by state and local governments may permit reimportation of drugs from foreign countries into the U.S., including foreign countries where the drugs are sold at lower prices than in the U.S., which could materially adversely affect our operating results.

We may face competition in the U.S. for our product candidates, if approved, from therapies sourced from foreign countries that have placed price controls on pharmaceutical products. In the U.S., the MMA contains provisions that may change U.S. importation laws and expand pharmacists' and wholesalers' ability to import cheaper versions of an approved drug and competing products from Canada, where there are government price controls. Further, the MMA provides that these changes to U.S. importation laws will not take effect unless and until the Secretary of HHS certifies that the changes will pose no additional risk to the public's health and safety and will result in a significant reduction in the cost of products to consumers. On September 23, 2020, the Secretary of HHS made such certification to Congress, and on October 1, 2020, the FDA published a final rule that allows for the importation of certain prescription drugs from Canada. Under the final rule, States and Indian Tribes, and in certain future circumstances pharmacists and wholesalers, may submit importation program proposals to the FDA for review and authorization. Since the issuance of the final rule, on November 23, 2020, several industry groups filed federal lawsuits in the U.S. District Court for the District of Columbia, requesting injunctive relief to prevent implementation of the rule. If implemented, importation of drugs from Canada and the MFN Model, as further discussed above, may materially and adversely affect the price we receive for any of our product candidates. We will continue to monitor developments and their potential effect on our business. We may face competition in the U.S. for our development candidates and investigational medicines, if approved, from therapies sourced from foreign countries that have placed price controls on pharmaceutical products. In the U.S., the FDA issued a final guidance document outlining a pathway for manufacturers to obtain an additional National Drug Code ("NDC") for an FDA-approved drug that was originally intended to be marketed in a foreign country and that was authorized for sale in that foreign country. The market implications of the final guidance are unknown at this time. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances.

On July 9, 2021, President Biden signed an executive order directing the FDA to coordinate with state and local entities to work on importing prescription drugs from Canada. Legislation or regulations allowing the reimportation of drugs, if enacted, could decrease the price we receive for any products that we may develop and adversely affect our future revenues and prospects for profitability. Such legislation, regulations, and executive action allowing the importation or reimportation of drugs could decrease the price we receive for any products that we may develop and adversely affect our future revenues and prospects for profitability.

If any of our product candidates receive marketing approval and we or others later identify undesirable side effects caused by the product candidate, our ability to market and derive revenue from the product candidates could be compromised.

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

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

Inadequate funding for the FDA, the SEC, and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel, and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC, and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to review and process our regulatory submissions timely, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital to properly capitalize and continue our operations.

Separately, in response to the COVID-19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities while local, national, and international conditions warrant. Since March 2020 when foreign and domestic inspections were largely placed on hold, the FDA has been working to resume routine surveillance, bioresearch monitoring, and pre-approval inspections on a prioritized basis. The FDA has developed a rating system to assist in determine when and where it is safest to conduct prioritized domestic inspections and resumed inspections in China and India in early 2021. In April 2021, the FDA issued guidance for industry formally announcing plans to employ remote interactive evaluations, using risk management methods, to meet user fee commitments and goal dates. Should the FDA determine that an inspection is necessary for

approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be appropriate, the agency has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information to make a determination on the acceptability of a facility, the FDA may defer action on the application until an inspection can be completed. In 2020, several companies announced the receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities.

Risks Related to Our Common Stock

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

Our stock price has historically fluctuated widely and is likely to continue to be volatile. From January 30, 2014, the first day of trading of our common stock, through June 30, 2021, the closing sale price of our common stock has ranged between a high of $46.00 per share and a low of $2.45 per share. The market price for our common stock may be influenced by many factors, including the other risks described in this "Risk Factors" section, and the following:

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

- terrorist acts, acts of war, or periods of widespread civil unrest;
- shifts in the political environment and changes in the government and agency leadership positions in connection with the 2020 presidential election as well as future election cycles;
- natural disasters and other calamities, including the COVID pandemic;
- general economic, industry, and market conditions; and
- developments concerning complaints or litigation against us.

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

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

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

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

As of June 30, 2021, our executive officers and directors, together with holders of five percent or more of our outstanding common stock and their respective affiliates, beneficially owned, in the aggregate, approximately 39.9% of our outstanding common stock, including shares subject to outstanding options that are exercisable within 60 days after such date, based on the Forms 3 and 4 and Schedules 13D and 13G filed by them with the SEC. As a result, these stockholders, if acting together, will continue to have significant influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation, or sale of all or substantially all of our assets, and any other significant corporate transaction. The interests of these stockholders may not be the same as, or may even conflict with, the interests of our other stockholders. For example, these stockholders could delay or prevent a change of control of our Company, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our Company or our assets and might affect the prevailing market price of our common stock. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

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

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

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

- the authority of the Board of Directors to issue preferred stock, such as the Redeemable Convertible Preferred, with such terms as the Board of Directors may determine.

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

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

As a public company, we incur, and we will continue to incur significant legal, accounting, and other expenses.

The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Select Market, and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly. Furthermore, 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.

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 common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our common stock will be the sole source of gain of our common stockholders for the foreseeable future.

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

Our stock price has fluctuated and may fluctuate for many reasons, including as a result of public announcements regarding the progress of our development efforts or the development efforts of our collaborators or competitors, the addition or departure of our key personnel, variations in our quarterly operating results, and changes in market valuations of pharmaceutical and biotechnology companies. This risk is especially relevant to us because pharmaceutical and biotechnology companies have experienced significant stock price volatility in recent years. When the market price of a stock has been volatile as our stock price has been and may be, holders of that stock have occasionally brought securities class action litigation against the company that issued the stock. We expect that the price volatility and class action lawsuits in the pharmaceutical and biotechnology industries 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. 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 and Board of Directors.

Our bylaws contain exclusive forum provisions, which may limit a stockholder's ability to bring a claim in a judicial forum it finds favorable and may discourage lawsuits with respect to such claims.

We most recently amended our bylaws in March 2021. 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 state law claims for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, or other employees to us or our stockholders, any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, as amended, our amended and restated certificate of incorporation or our amended and restated bylaws, any action to interpret, apply, enforce, or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws, any action to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws, or any other action asserting a claim against us that is governed by the internal affairs doctrine (we refer to the foregoing provision as the Delaware Forum Provision). The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Exchange Act. Our amended and restated bylaws further provide that, unless we consent in writing to an alternative forum, the district courts of the United States shall be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act or the Federal Forum Provision. In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any

interest in shares of our capital stock is deemed to have notice of and consented to the foregoing Delaware Forum Provision and the Federal Forum Provision; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the U.S. federal securities laws and the rules and regulations thereunder.

We recognize that the Delaware Forum Provision and the Federal Forum Provision may impose additional litigation costs on stockholders who assert the provision is not enforceable and may impose more general additional litigation costs in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware in the event of claims governed by the Delaware Forum Provision. Additionally, these forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers, or employees, which may discourage such lawsuits against us and our directors, officers, and employees even though an action, if successful, might benefit our stockholders. While the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court are "facially valid" under Delaware law, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert the provision is unenforceable, and if the Federal Forum Provision is found to be unenforceable, we may incur additional costs with resolving such matters. The Court of Chancery of the State of Delaware and the United States district courts may also reach different judgments or results than would other courts, including courts where a stockholder considering an actions may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

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

In April 2017, we issued 700,000 shares of the Redeemable Convertible Preferred in a private placement, which were convertible into shares of our common stock at an agreed conversion rate. In December 2017, all shares of Redeemable Convertible Preferred were converted into shares of our common stock. We granted the holders of Redeemable Convertible Preferred certain demand, shelf, and "piggyback" registration rights with respect to the shares of common stock issued upon conversion of the Redeemable Convertible Preferred. Such registration rights continue subsequent to the conversion and repurchase of the Redeemable Convertible Preferred with respect to the shares of common stock issued in such conversion. In accordance with such registration rights, we filed a shelf registration statement on Form S-3 covering the resale of 24,491,663 shares of our common stock by the former holders of Redeemable Convertible Preferred. The registration statement was declared effective on May 9, 2018, and all shares of common stock issued upon conversion of the Redeemable Convertible Preferred may now be freely sold in the open market. Additionally, we issued 983,208 shares of our common stock to Alnylam in April 2018, 835,834 shares of our common stock to Alexion in October 2018, 5,414,185 shares of our common stock to Lilly in December 2018, and 2,279,982 shares of our common stock to Novo in December 2019. The sale of a significant amount of these shares in the open market or the perception that these sales may occur could cause the market price of our common stock to decline or become highly volatile.

General Risks

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

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

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

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse 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 stockholders may experience significant dilution as a result of future equity offerings and exercise of outstanding options.

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 shares, which were converted into common stock in December 2017 and with the follow-on offerings of our common stock in December 2017 and September 2018. We cannot assure you that we will be able to sell shares or other securities in any offering at a price per share that is equal to or greater than the price paid by our existing shareholders, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock or other securities

convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share paid by our existing stockholders.

In addition, we have a significant number of securities allowing for the purchase of our common stock. As of August 2, 2021, we also had 7,840,275 shares of common stock reserved for future issuance under our stock incentive plans. As of that date, there were also stock options to purchase 14,199,163 shares of our common stock and 1,241,807 restricted stock units outstanding. The exercise of outstanding options having an exercise price per share that is less than the offering price per share paid by our existing stockholders will increase dilution to such stockholders.

On May 6, 2021, we entered into a Sales Agreement with Cowen and Company, LLC, as sales agent, to provide for the offering, issuance, and sale by us of up to $200.0 million of our common stock from time to time, including in "at-the-market" offerings under our universal shelf registration statement on Form S-3 that we filed on November 7, 2019. The sale and issuance of our common stock under this facility would result in dilution to our stockholders.

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

Sales of a substantial number of shares of our common stock in the public market, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. As of August 2, 2021, we had 77,734,172 shares of common stock outstanding, all of which, other than shares held by our directors and certain officers, were eligible for sale in the public market, subject in some cases to compliance with the requirements of Rule 144, including the volume limitations and manner of sale requirements. In addition, shares of common stock issuable upon exercise of outstanding options and shares reserved for future issuances under our stock incentive plans will become eligible for sale in the public market to the extent permitted by applicable vesting requirements and subject in some cases to compliance with the requirements of Rule 144.

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

(a) Unregistered Sales of Equity Securities

Not applicable.

(b) Use of Proceeds

Not applicable.

(c) Issuer Purchases of Equity Securities

In connection with the vesting of restricted stock units granted to employees, we withheld certain shares with values equivalent to employees' minimum statutory obligations for the applicable income and other employment taxes.

A summary of the shares withheld to satisfy employee tax withholding obligations for the three months ended June 30, 2021 is as follows:

Period	Total Number of Shares Purchased	Average Price Paid per Share	Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs	Maximum Number of Shares That May Yet Be Purchased Under The Plan
04/01/21 - 04/30/21	343	$ 31.19	—	—
05/01/21 - 05/31/21	—	$ —	—	—
06/01/21 - 06/30/21	12,616	$ 35.74	—	—
Total	12,959	$ 35.67	—	—

ITEM 3. DEFAULTS UPON SENIOR SECURITIES

Not applicable.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

ITEM 5. OTHER INFORMATION

None.

ITEM 6. EXHIBITS

Exhibit Number	Description of Documents	Incorporated by Reference			
		Form	File Number	Exhibit	Filing Date
3.1	Amended and Restated Certificate of Incorporation of the Company.	8-K	001-36281	3.1	February 5, 2014
3.2	Amended and Restated Bylaws of the Company.	8-K	001-36281	3.2	March 12, 2021
10.1	Royalty Acquisition Agreement by and between the Company and Royalty Pharma PLC, dated as of April 8, 2021.	10-Q	001-36281	10.1	May 6, 2021
31.1*	Certification of the Company's principal executive officer required by Rule 13a-14(a) or Rule 15d-14(a).				
31.2*	Certification of the Company's principal financial officer required by Rule 13a-14(a) or Rule 15d-14(a).				
32.1**	Section 1350 Certifications.				
101.INS*	XBRL Report Instance Document				
101.SCH*	XBRL Taxonomy Extension Schema Document				
101.CAL*	XBRL Taxonomy Calculation Linkbase Document				
101.LAB*	XBRL Taxonomy Label Linkbase Document				
101.PRE*	XBRL Taxonomy Presentation Linkbase Document				
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document				
104*	Cover Page Interactive Data File (formatted as Inline XBRL and included in Exhibit 101).				

* Filed herewith.

** Exhibit 32.1 is being furnished and shall not be deemed to be "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liability of that section, nor shall such exhibit be deemed to be incorporated by reference in any registration statement or other document filed under the Securities Act or the Exchange Act, except as otherwise stated in such filing.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

DICERNA PHARMACEUTICALS, INC.

Date: August 9, 2021

By: /s/ Douglas W. Pagán

Douglas W. Pagán

Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)

Exhibit 31.1

CERTIFICATIONS

I, Douglas M. Fambrough, III, Ph.D., certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Dicerna Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 9, 2021

/s/ Douglas M. Fambrough, III, Ph.D.

Douglas M. Fambrough, III, Ph.D.
President, Chief Executive Officer and Director

Exhibit 31.2

CERTIFICATIONS

I, Douglas W. Pagán, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Dicerna Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under my supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 9, 2021

/s/ Douglas W. Pagán

Douglas W. Pagán
Chief Financial Officer

Exhibit 32.1

SECTION 1350 CERTIFICATIONS*

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. § 1350), Douglas M. Fambrough, III, Ph.D., Chief Executive Officer and Director of Dicerna Pharmaceuticals, Inc. (the "Company"), and Douglas W. Pagán, Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

1. The Company's Quarterly Report on Form 10-Q, for the quarter ended June 30, 2021, to which this Certification is attached as Exhibit 32.1 (the "Quarterly Report"), fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

2. The information contained in the Quarterly Report fairly presents, in all material respects, the financial condition and results of operations of the Company for the period covered by the Quarterly Report.

Dated: August 9, 2021

/s/ Douglas M. Fambrough, III, Ph.D.
Douglas M. Fambrough, III, Ph.D.

President, Chief Executive Officer and Director

/s/ Douglas W. Pagán

Douglas W. Pagán
Chief Financial Officer

* This certification accompanies the Quarterly Report on Form 10-Q, to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing.